UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE: JOHNSON & JOHNSON TALCUM POWDER PRODUCTS MARKETING, SALES PRACTICES AND PRODUCTS LIABILITY LITIGATION	MDL Docket No. 2738
This Document Relates To All Cases	

DEFENDANTS JOHNSON & JOHNSON AND JOHNSON & JOHNSON CONSUMER INC.'S MEMORANDUM OF LAW IN SUPPORT OF MOTION TO EXCLUDE PLAINTIFFS' EXPERTS' OPINIONS RELATED TO BIOLOGICAL PLAUSIBILITY

DRINKER BIDDLE & REATH LLP
A Delaware Limited Liability Partnership
600 Campus Drive
Florham Park, New Jersey 07932
(973) 549-7000

SKADDEN, ARPS, SLATE, MEAGHER & FLOM LLP
1440 New York Avenue, N.W.
Washington, D.C. 20005
(202) 371-7000

Attorneys for Defendants Johnson & Johnson and Johnson & Johnson Consumer Inc.

TABLE OF CONTENTS

Page

TABLE OF AUTHORITIES

Page(s)

FEDERAL CASES

STATE CASE

FEDERAL REGULATION

OTHER AUTHORITIES

Plaintiffs' experts' biological plausibility opinions depend on three unsupported hypotheses: (1) that talc can magically migrate from the external perineum into the vagina, up the cervix and into the fallopian tubes or ovaries; (2) that perineal talc use can cause chronic inflammation in the female genitourinary tract (even though no pathologist has ever reported seeing such a reaction); and (3) that chronic inflammation can cause ovarian cancer (even though the relevant evidence is to the contrary). These opinions should be excluded in their entirety under *Daubert* and Rule 702.[1]

---

[1] Plaintiffs' experts Drs. Shawn Levy and Judith Zelikoff purport to limit their opinions to the issue of biological plausibility, and this brief seeks to exclude their opinions in their entirety. Plaintiffs' experts Drs. Arch Carson, Daniel Clarke-Pearson, Sarah Kane, Anne McTiernan, Patricia Moorman, Laura Plunkett, Jack Siemiatycki, Sonal Singh, Rebecca Smith-Bindman, Ellen Blair Smith and Judith Wolf opine on biological plausibility as part of broader opinions on causation and/or regulatory issues; this brief only addresses their biological plausibility opinions (*see* Expert Report of Arch Carson, M.D., Ph.D. ("Carson Rep.") at 4-5, 7-8, 10, Nov. 16, 2018 (attached as Ex. C9 to Omnibus Certification of Julie Tersigni, Esq. ("Tersigni Cert.")); Expert Report of Daniel L. Clarke-Pearson ("Clarke-Pearson Rep.") at 9, Nov. 16, 2018 (attached as Ex. C14 to Tersigni Cert.); Expert Report of Sarah E. Kane, M.D. ("Kane Rep.") at 4, 9-15, 35-36, Nov. 15, 2018 (attached as Ex. C38 to Tersigni Cert.); Expert Report of Anne McTiernan, M.D., Ph.D. ("McTiernan Rep.") at 58-63, 66-67, Nov. 16, 2018 (attached as Ex. C7 to Tersigni Cert.); Expert Report of Patricia G. Moorman, M.S.P.H., Ph.D. ("Moorman Rep.") at 32-37, Nov. 16, 2018 (attached as Ex. C35 to Tersigni Cert.); Expert Report of Laura M. Plunkett, Ph.D., D.A.B.T. ("Plunkett Rep.") at 19-20, 28-48, 52, 77, Nov. 16, 2018 (attached as Ex. C28 to Tersigni Cert.); Expert Report of Jack Siemiatycki, M.Sc. ("Siemiatycki Rep.") at 64-66, Nov. 16, 2018 (attached as Ex. C21 to Tersigni Cert.); Expert Report of Sonal Singh, M.D., M.P.H., ("Singh Rep.") at 57-60, Nov. 16, 2018 (attached as Ex. C40 to Tersigni Cert.); Expert Report of Rebecca Smith-Bindman, M.D. ("Smith-

(cont'd)

Plaintiffs' own supposed "evidence" only highlights the weakness of their theories. Most notably:

- The 2018 Draft Screening Assessment by Health Canada, on which plaintiffs' counsel heavily relied in depositions of defense experts, expressly states that "***the specific mechanism(s) and cascade of molecular events by which talc might cause ovarian cancer have not been identified***."[2]

- The 2018 unpublished manuscript by Mohamed Taher that forms the basis of the Health Canada draft assessment acknowledges that "[d]ata on talc migration in the genital tract of animals ***is inconsistent***" and concludes that chronic inflammation is merely a "***possible*** mechanism[]."[3]

(cont'd from previous page)
Bindman Rep.") at 35, 40, Nov. 15, 2018 (attached as Ex. C36 to Tersigni Cert.); Expert Report of Ellen Blair Smith, M.D. ("Smith Rep.") at 16-18, 20, Nov. 16, 2018 (attached as Ex. C16 to Tersigni Cert.); Expert Report of Judith Wolf, M.D. ("Wolf Rep.") at 10-13, 15, Nov. 16, 2018 (attached as Ex. C23 to Tersigni Cert.)), although defendants seek to exclude their opinions in their entirety, as set forth in defendants' Memorandum in Support of Motion to Exclude Plaintiffs' Experts' Opinions on General Causation and defendants' Memorandum in Support of Motion to Exclude Plaintiffs' Experts' Opinions Unrelated to General Causation, submitted herewith. Finally, plaintiffs' expert Dr. Ghassan Saed's opinions are primarily addressed in defendants' Memorandum in Support of Motion to Exclude Expert Opinions of Ghassan Saed ("Saed Mem."), but his opinions broadly concern biological plausibility, and as such, should be excluded for the reasons set forth in this brief as well.

[2] *See* Health Canada, Draft Screening Assessment: Talc ($Mg_3H_2(SiO_3)_4$) 21 (Chem. Abstracts Serv. Registry No. 14807-96-6) (2018) ("Draft Screening Assessment") (attached as Ex. A58 to Tersigni Cert.) (emphasis added).

[3] Taher et al., *Systematic Review and Meta-Analysis of the Association Between Perineal Use of Talc and Risk of Ovarian Cancer* 24, 26 (2018) (unpublished manuscript) ("Taher 2018") (attached as Ex. A137 to Tersigni Cert.).

- The 2018 meta-analysis by Penninkilampi on which many of plaintiffs' experts rely expressly states that "***the evidence remains insufficient to understand*** the mechanisms [by which talc purportedly causes ovarian cancer] with any reasonable certainty."[4]

And plaintiffs' own expert, Dr. Zelikoff, similarly acknowledged that the "mechanism by which perineal talc use may increase the risk of ovarian cancer is uncertain"[5] and that she does not know of "any medical or scientific community that has accepted that there is biologic plausibility of talcum powder products causing ovarian cancer."[6]

Nevertheless, plaintiffs' experts characterize these unsubstantiated hypotheses as "widely accepted," "accepted widely," or supported by "robust data," "considerable evidence" or a "significant body of evidence."[7] These characterizations are based on fantasy, not science.

First, plaintiffs' experts fail to address the biological plausibility question in a methodical manner because they conflate the different subtypes of ovarian cancer

---

[4] Penninkilampi & Eslick, *Perineal Talc Use and Ovarian Cancer: A Systematic Review and Meta-Analysis*, 29 Epidemiol. 41, 45 (2018) ("Penninkilampi & Eslick 2018") (attached as Ex. A109 to Tersigni Cert.) (emphasis added) (cited by all of plaintiffs' experts other than Drs. Campion, Cook, Crowley, Longo/Rigler, Krekeler and Zambelli-Weiner).

[5] (Dep. of Judith Zelikoff, Ph.D. ("Zelikoff Dep.") 400:3-5, Jan. 21, 2019 (attached as Ex. B31 to Tersigni Cert.) (quoting Penninkilampi & Eslick 2018).)

[6] (*Id.* 157:2-16.)

[7] (Smith-Bindman Rep. at 12; Smith Rep. at 20; Moorman Rep. at 33; Siemiatycki Rep. at 65; Singh Rep. at 65.)

when doing so is convenient to their theories. For example, many of plaintiffs' experts inappropriately rely on literature related to specific subtypes of ovarian cancer to reach conclusions about ovarian cancer in general. The problem with this approach is that "ovarian cancer" comprises several distinct diseases that involve mutations of different genes, develop in different tissues and have different risk factors and causes. Without specifying which subtype(s) of ovarian cancer is/are supposedly caused by perineal talc exposure, plaintiffs' experts cannot even begin to research or address this question in a scientifically methodological manner.

Second, plaintiffs' experts lack reliable scientific evidence that externally applied talc can enter the body and travel all the way to the fallopian tubes or ovaries. Plaintiffs' experts rely heavily on studies in which substances were injected into the vagina, often while the subject was supine with legs up. Needless to say, such studies do not prove that talc applied externally enters the vagina, against gravity and the body's defense mechanisms, and travels to the ovaries or fallopian tubes. As the International Agency for Research on Cancer ("IARC") concluded in 2010, "the evidence for retrograde transport of talc to the ovaries in normal women is ***weak***," and animal studies – including those relied on by

plaintiffs' experts in this litigation – "showed ***no evidence*** of retrograde transport of talc to the ovaries."[8]

Third, even if it were plausible that cosmetic talc migrates from the perineum to the ovaries or fallopian tubes, there is no reliable scientific evidence that it causes chronic inflammation in the female genitourinary tract or that such chronic inflammation can cause ovarian cancer. As plaintiffs' own toxicologist, Dr. Zelikoff, has admitted, there are ***no*** peer-reviewed studies that have reported chronic inflammation in the genitourinary tract of women with a history of perineal talc use.[9] Further, studies identifying talc in ovarian tissue (of both users and non-users of cosmetic talc) have not found chronic inflammation in the area of the talc.[10] Indeed, defendants' expert, Dr. Robert Kurman, a renowned gynecological pathologist, has "examined a number of surgical pathology specimens from plaintiffs in talc litigation" but has never observed inflammation associated with talc use.[11]

---

8 *See* Int'l Agency for Research on Cancer, World Health Org., 93 *Monograph on the Evaluation of Carcinogenic Risks to Humans: Carbon Black, Titanium Dioxide, and Talc* 411 (2010) (attached as Ex. A72 to Tersigni Cert.).

9 (Zelikoff Dep. 356:13-358:4.)

10 Heller et al., *The Relationship Between Perineal Cosmetic Talc Usage and Ovarian Talc Particle Burden*, Am. J. Obstet Gynecol 1507 (1996) ("Heller 1996 – Talc") (attached as Ex. A60 to Tersigni Cert.).

11 (Expert Report of Robert J. Kurman, M.D. ("Kurman Rep.") at 17, Feb. 25, 2019 (attached as Ex. C37 to Tersigni Cert.).)

In any event, the published literature evaluating a potential link between chronic inflammation and ovarian cancer is either inconclusive or tends to ***disprove*** such a link. While plaintiffs' experts rely on cherry-picked statements from various review articles, epidemiological research (that did not test effects of inflammation) or papers addressing inflammation and cancer generally to suggest that the posited link between inflammation and ovarian cancer is established, those studies make clear that the authors have merely ***proposed*** a connection and assert that more research is needed to determine whether it exists. Further, the relevant science demonstrates that, if anything, ovarian cancer causes inflammation, not the other way around. And plaintiffs' other mechanism theory – that talc increases the risk of cancer by suppressing MUC1 antibodies – is similarly unsupported by the relevant scientific literature.

Fourth, and finally, Dr. Zelikoff's biological plausibility opinions are separately unreliable because her report is rife with plagiarism, significantly undermining the credibility of her methodology.

ARGUMENT

As set forth in defendants' motion to exclude plaintiffs' general causation opinions, biological plausibility is one of the considerations included in the Bradford Hill framework for assessing causation. "While *Daubert* does not require absolute precision in identifying the medical mechanism of injury, there still must

be 'sufficiently compelling proof'" of that mechanism. *Soldo v. Sandoz Pharm. Corp.*, 244 F. Supp. 2d 434, 561-62 (W.D. Pa. 2003) (citation omitted). "[A] biological explanation without evidence of the mechanism by which it works is merely ***an unproven hypothesis, a theory***," not a plausible theory of causation. *In re Accutane Prods. Liab.*, 511 F. Supp. 2d 1288, 1295-96 (M.D. Fla. 2007) (excluding causation opinion of gastroenterologist who conceded that "the exact biological mechanism by which [inflammatory bowel disease] occurs" had not been established by science but sought to testify about "possible mechanisms" by which a medication could cause the disease; because "none of [the] 'three possible mechanisms' have been tested or proven," they could not support causation) (citation omitted).

In assessing biological plausibility, courts have recognized that an expert must be able to show that the allegedly dangerous substance "behaves in the hypothesized way in the real world." *In re Nexium (Esomeprazole) Prods. Liab. Litig.*, No. ML 12-2404 DSF (SSx), 2014 WL 5313871, at *3 (C.D. Cal. Sept. 30, 2014), *aff'd*, 662 F. App'x 528 (9th Cir. 2016). In *Nexium*, for example, the court excluded a general causation opinion expressly formulated pursuant to the Bradford Hill framework because, among other reasons, the expert had failed to establish a biologically plausible mechanism of injury. There, the expert posited that proton-pump inhibitors ("PPIs") like Nexium could cause osteoporosis

("OP"). *Id.* But while the expert offered "several hypothetical mechanisms for PPI causation of OP," he did "not present any evidence that Nexium behaves in the hypothesized way in the real world." *Id.* Pointing to the expert's principal hypothesis that Nexium could cause OP by reducing calcium uptake, the court illustrated the problem by explaining that the expert "provide[d] no studies, either in the literature or that he, himself, conducted that purport to demonstrate that Nexium, or PPIs generally, reduce calcium uptake." *Id.*; *see also Glastetter v. Novartis Pharm. Corp.*, 252 F.3d 986, 989 (8th Cir. 2001) (per curiam); *accord In re Viagra Prods. Liab. Litig.*, 658 F. Supp. 2d 950, 959-60 (D. Minn. 2009) (excluding biological plausibility theory that was "labeled a hypothesis," and which the authors acknowledged remained "untested"); *In re Propulsid Prods. Liab. Litig.*, 261 F. Supp. 2d 603, 616 (E.D. La. 2003) (excluding expert testimony on causation for lack of reliable evidence of a plausible biological mechanism where literature noted that the "mechanism causing [the condition] is 'unknown at this time'") (citation omitted); *Henricksen v. ConocoPhillips Co.*, 605 F. Supp. 2d 1142, 1175-76 (E.D. Wash. 2009) (striking causation experts who lacked reliable evidence that it was "biological[ly] plausibl[e]" that the defendant's benzene-containing gasoline was capable of causing acute myelogenous leukemia ("AML"); the "studies relied upon by [p]laintiffs make clear that the connection

between gasoline or the benzene component of gasoline and AML is at this point in time ***only a hypothesis in need of further investigation***") (emphasis added).

Plaintiffs' experts' biological mechanism theories do not meet these standards, for all the reasons set forth below.

I. PLAINTIFFS' EXPERTS' BIOLOGICAL PLAUSIBILITY THEORIES PROCEED FROM THE ERRONEOUS PREMISE THAT OVARIAN CANCER IS A UNITARY DISEASE.

Plaintiffs' experts' biological plausibility opinions are fundamentally unreliable because they do not account for the fact that ovarian cancer is a term used for multiple diseases, each of which likely has different causes.

It is well-recognized by the scientific community that ovarian cancer is not a single disease, but rather a series of different cancers arising from different tissues and different gene mutations, and associated with different risk factors.[12] In fact, several of plaintiffs' experts recognize that there are multiple "distinct" and "heterogeneous" ovarian cancer subtypes.[13]

---

[12] (*See, e.g.*, Expert Report of Benjamin M. Neel, M.D., Ph.D. ("Neel Rep.") at 12, Feb. 25, 2019 (attached as Ex. C10 to Tersigni Cert.) (explaining that "ovarian cancer arises in different cell types as a consequence of distinct mutational events," and "different subtypes of the disease are associated with different risk factors"); Expert Report of Michael Birrer, M.D., Ph.D. ("Birrer Rep.") at 3, Feb. 25, 2019 (attached as Ex. C33 to Tersigni Cert.) (further explaining that the different subtypes are "characterized by completely different patterns of genomic alterations and different developmental origins," and exhibit "different microscopic appearances, biologic characteristics and clinical features").)

[13] (*See* Expert Report of Judith Zelikoff, Ph.D. ("Zelikoff Rep.") at 19, Nov.

(cont'd)

As Dr. Benjamin Neel, the head of cancer research for NYU Langone, has explained, "ovarian cancer" is generally broken down into "epithelial" and "non-epithelial" cancers.[14] Epithelial ovarian cancers include: (1) high grade serous ovarian cancer ("HGSOC"); (2) low grade serous ovarian cancer ("LGSOC"); (3) mucinous carcinoma; (4) endometrioid carcinoma; and (5) clear cell carcinoma.[15] Non-epithelial cancers include germ cell tumors, and sex cord-stromal tumors.[16] Most, if not all, HGSOC originates from the fimbria (fringe tissue) of the fallopian tube (LGSOC likely does as well, though the evidence is less clear).[17] By contrast, endometrioid and clear cell carcinoma likely arise from endometriotic lesions and mucinous carcinomas from the junction of the

---

(cont'd from previous page)

16, 2018 (attached as Ex. C24 to Tersigni Cert.) ("Ovarian cancer comprises at least five distinct histological subtypes . . . ."); Smith-Bindman Rep. at 9 ("Ovarian cancers . . . are a heterogeneous group of malignancies that vary in their pathological appearance, molecular biology, risk factors, etiology, and prognosis.").)

[14] Epithelial tissues are tissues lining organs. (*See generally* Neel Rep. at 9.)

[15] (*Id.* at 10.)

[16] (*Id.*) About 60-65% of "ovarian cancer" is HGSOC; the other epithelial cancers account for approximately 25-30%; and non-epithelial cancers the remainder. (*See id.* at 10.) Plaintiffs do not generally allege that non-epithelial ovarian cancers are caused by talc use.

[17] (*Id.* at 10-11.)

peritoneum and fallopian tube, or possibly from sites outside the reproductive system.[18]

Although the various subtypes of ovarian cancer originate from different tissues, they (like all cancers) arise as a result of genetic mutations.[19] *See, e.g.*, *Carl v. Johnson & Johnson*, Nos. ATL-L-6546-14, ATL-L-6540-14, 2016 WL 4580145, at *14 (N.J. Super. Ct. Law Div. Sept. 2, 2016) (it is "universally accepted that mutations in critical genes is the mechanism that causes cancer"), *appeal pending*.[20] But different genetic mutations are implicated in the various subtypes.[21] For example, the TP53 gene – considered the most important tumor-suppressor gene – is mutated or deleted in HGSOC, but is only rarely implicated in the development of the other types of epithelial ovarian cancer.[22] As Dr. Neel

---

18 (*Id.*; *see also generally* Kurman Rep. at 5-11.)

19 The genetic origin of ovarian cancers casts serious doubt on the entire notion that talc could cause ovarian cancer since talc "is chemically inert and non-genotoxic." (Neel Rep. at 14; *see also* Saed Mem. at 46-47.)

20 As Dr. Neel explains, these can involve "gain of function" mutations, which result in increased cell growth, division and longevity, or "loss-of-function mutations" to tumor-suppressor genes, which, if functioning properly, inhibit cancer development by, for example, telling cells to stop dividing or by repairing damaged DNA. (Neel Rep. at 5-6.) Most cancers "result from DNA damage or errors in replication that . . . accumulate over time," which is why "the greatest contributor to cancer risk is age." (*Id.* at 7-8.)

21 (*See* Expert Report of Dr. Shawn Levy, Ph.D. ("Levy Rep.") at 6 (attached as Ex. C39 to Tersigni Cert.) ("Certain specific genetic and transcriptional signatures are associated with each histological subtype.").)

22 (Neel Rep. at 11-12; Birrer Rep. at 3-4; *see also* Levy Rep. at 6 (identifying *(cont'd)*

explains, the "differences in the genetic architecture of different tumors also imply distinct underlying mutational processes," and it is "highly unlikely that tumors that have different genomic defects [and] mutational signatures are caused by the same mutational agents."[23]

Given the different genes and tissues implicated in the different subtypes of ovarian cancer, different risk factors are unsurprisingly associated with different subtypes of EOC. For example, endometriosis (a condition involving abnormal growth of uterine tissue) is a risk factor for clear cell and endometrial ovarian cancer, but not other ovarian cancer subtypes.[24] Similarly, smoking is a risk factor for mucinous ovarian cancer, but no other subtypes, and obesity is a risk factor for several subtypes of ovarian cancer, but not HGSOC.[25] In addition, gynecologic procedures such as hysterectomy and bilateral tubal ligation have been shown to reduce the risk of clear cell and endometrial ovarian cancer, with lesser effects on HGSOC.[26] For these reasons, as Dr. Neel opines, any putative expert analysis

---

(cont'd from previous page)
different mutations associated with LGSOC, endometrioid and clear cell carcinoma).) HGSOC is in fact "genetically . . . more similar to triple negative breast cancer than to other types of ovarian cancer." (Neel Rep. at 10.)

23 (Neel Rep. at 10.)

24 (Levy Rep. at 13-14; Neel Rep. at 13; Birrer Rep. at 18; *see also* Kurman Rep. at 9-10.)

25 (Neel Rep. at 14.)

26 (*Id.*; Kurman Rep. at 9; Birrer Rep. at 9-10.)

"that treat[s] 'ovarian cancer' as a single entity, should . . . be viewed with skepticism."[27]

Plaintiffs' experts, however, do just that, intoning that talc generally causes all types of "ovarian cancer" (or at least all types of epithelial ovarian cancer) via chronic inflammation.[28] For example, Dr. Zelikoff dedicates seven pages of her report to describing various elements of the supposed "mechanism of inflammation," but does not even mention how the various components of her theory would operate to trigger the "distinct" ovarian cancer subtypes she

---

[27] (Neel Rep. at 12 (emphasis omitted).)

[28] (*E.g.*, Smith Rep. at 3 (considering "cancers of the ovary, fallopian tubes, and peritoneum to be a single entity," "[a]ll [of which] are associated with talcum powder use"); Expert Report of Ghassan Saed, Ph.D. ("Saed Rep.") at 3-4, Nov. 16, 2018 (attached as Ex. C17 to Tersigni Cert.) ("In the last decade, researchers have proposed the theory that many ovarian cancers arise from the distal fallopian tubes. For this reason, as well as the similarities in pathogenesis, presentation, treatment, and prognosis, fallopian tube, ovarian, and peritoneal cancer are generally treated as a single entity."); Carson Rep. at 3 ("Ovarian, fallopian tube, and peritoneal cancers have a similar clinical presentation and are treated similarly, and current evidence suggests that they may have a common origin, supporting a common staging system."); Siemiatycki Rep. at 47 ("[T]here is no persuasive evidence in these studies, taken as a whole that the effect of talc differs by histologic subtype of epithelial ovarian cancer."); *see also, e.g.*, Kane Rep. at 35; Wolf Rep. at 11-13; Clarke-Pearson Rep. at 4; Smith-Bindman Rep. at 12-13; Levy Rep. at 11-13; McTiernan Rep. at 59-63; Moorman Rep. at 33-37; Singh Rep. at 58-59; Plunkett Rep. at 46 (all failing to address the different subtypes when analyzing biological plausibility); Zelikoff Dep. 193:11-195:7 (confirming that she did not analyze biological plausibility as to the different subtypes; based on her admittedly "cursory knowledge," "there are definite commonalities in terms of the induction of ovarian types of cancer").)

elsewhere acknowledges exist, much less mutations in the subtypes' signature genes.[29] And Dr. Levy, who elsewhere in his report acknowledges the distinctions between subtypes and the gene mutations associated with them,[30] likewise fails to address their significance in his discussion of "[t]he role of inflammation in ovarian cancer."[31] Instead, his discussion cites examples of inflammatory conditions supposedly "associated with ovarian cancer" that are actually linked only to specific subtypes. For example, he contends that "inflammation explains the association between endometriosis and epithelial ovarian cancer,"[32] when, in fact, "[e]ndometriosis is a risk factor . . . only for" endometrioid and clear cell carcinoma,[33] and "is not associated with an increased risk of" HGSOC.[34] Tellingly, Dr. Levy is also apparently unfamiliar with current scientific thinking,

---

29 (Zelikoff Rep. at 6, 21-27.)

30 (Levy Rep. at 6.)

31 (*Id.* at 11-13.)

32 (*Id.* at 12.)

33 (Neel Rep. at 13.)

34 (Birrer Rep. at 18.) Similarly, although Dr. Siemiatycki testified at his deposition that he believes "it becomes very fragile to draw inferences about [non-serous] [sub]types," he assumes "that all ovarian cancers are affected the same way." (*See, e.g.*, Dep. of Jack Siemiatycki, Ph.D. 204:2-13, Jan. 31, 2019 (attached as Ex. B29 to Tersigni Cert.).) Like plaintiffs' other experts, his discussion of biological plausibility makes no mention of the different subtypes of ovarian cancer. (Siemiatycki Rep. at 64-66.)

which rejects inflammation as the likely explanation for the link between endometriosis and certain subtypes of ovarian cancer. As Dr. Kurman explains:

> [E]ndometriosis is often not accompanied by inflammation, and when it is, the inflammation is composed of lymphocytes and plasma cells, not foreign body granulomatous reactions like those associated with talc exposure. Moreover, based on the fact that shared molecular genetic changes have been found in endometriosis and endometrioid and clear cell carcinoma, the scientific evidence strongly suggests that endometriosis is a precursor lesion to these cancers, not a source of inflammation that causes them.[35]

Plaintiffs' experts' failure to address how their mechanism theories relate to the different ovarian cancer subtypes is especially problematic because many of the animal and in vitro studies they rely on to support their theories involved examinations of tissues or cells that are only implicated in the etiology of some ovarian cancer subtypes. For example, a number of plaintiffs' experts rely heavily on Dr. Ghassan Saed's experiments.[36] But among other cell types (including spleen macrophage cells, which are not relevant to any form of ovarian cancer),

---

[35] (Kurman Rep. at 16-17; *see also* Birrer Rep. at 18 (explaining that there is no evidence that the inflammation associated with endometriosis – rather than the displacement of endometrial cells that is a hallmark of the condition – is responsible for the increased risk of certain cancers in endometriosis patients).)

[36] (*E.g.*, Zelikoff Rep. at 25; Levy Rep. at 14.) Dr. Saed's opinions and experiments are unreliable and inadmissible for all the reasons set forth in defendants' motion to exclude his opinions. To the extent other plaintiffs' experts cite Dr. Saed's work to support various aspects of their biological plausibility opinions (*see, e.g.*, Kane Rep. at 11; Moorman Rep. at 34; Smith Rep. at 18), their opinions are unreliable for the same reasons.

Dr. Saed used immortalized fallopian tube and ovarian epithelial cells, which are uninformative with respect to endometrioid and clear cell carcinomas (since those cancers originate in uterine tissue, as noted above).[37] Further, the "ovarian cancer" cell lines used by Dr. Saed were not derived from HGSOCs, the most common and lethal subtype of ovarian cancer, but rather from endometrioid or unknown cancer subtypes.[38]

Similarly, as set forth below, another study that plaintiffs' experts rely on heavily – Buz'Zard and Lau 2007 – tested an immortalized granulosa cell line that is only possibly relevant to sex cord-stromal tumors (which can arise from granulosa tissues, and which several plaintiffs' experts do not even allege can be caused by talc).[39] That study also tested immortalized ovarian epithelial cells, which are not relevant to HGSOC (insofar as HGSOC is now understood to largely

---

[37] (*See* Saed Mem. at 45.)

[38] (Expert Report of Jeff Boyd, Ph.D. at 8, Feb. 25, 2019 (attached as Ex. C22 to Tersigni Cert.).)

[39] Buz'Zard & Lau, *Pycnogenol® reduces Talc-induced Neoplastic Transformation in Human Ovarian Cell Cultures*, 21 Phytother. Res. 579, 580 (2007) ("Buz'Zard & Lau 2007") (attached as Ex. A16 to Tersigni Cert.). (*See also, e.g.*, McTiernan Rep. at 17 (stating that "[o]nly epithelial ovarian cancer has been studied in relation to use of talcum powder products" and therefore that her report is referring to "'epithelial ovarian cancer'" wherever it uses the term "'ovarian cancer,'" thereby excluding sex cord-stromal tumors from the scope of her opinions).)

originate in the fallopian tubes), or to endometriosis and clear cell carcinoma (since they arise from cells originating in the uterine endometrium).

In short, plaintiffs' experts' failure to grapple with the fundamental differences among ovarian cancer subtypes makes their opinions unreliable because the notion that talc can somehow cause different diseases that are considered to have different etiologies by the scientific community is illogical and unscientific. *See, e.g.*, *In re Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig.*, 26 F. Supp. 3d 449, 463 (E.D. Pa. 2014) (excluding expert's causation opinion because, although the expert cited studies demonstrating that "Zoloft [was] significantly associated with septal defects in the heart," the expert's "opinion [wa]s not limited to [that] one injury"); *Siharath v. Sandoz Pharm. Corp.*, 131 F. Supp. 2d 1347, 1371 (N.D. Ga. 2001) (rejecting an opinion that because Parlodel causes ischemic strokes, it also causes hemorrhagic strokes; "ischemic strokes and hemorrhagic strokes are distinct and have different *modi operandi*" and causes); *Muzzey v. Kerr-McGee Chem. Corp.*, 921 F. Supp. 511, 515, 519 (N.D. Ill. 1996) (excluding experts who "assert[ed] that because radiation exposure causes Chronic Myelogenous Leukemia ('CML'), another myeloproliferative disease, radiation exposure probably also causes all other myeloproliferative diseases"); *Davis v. Sec'y of Health & Human Servs.*, No. 07-451V, 2010 WL 1444056, at *13 (Fed. Cl. Mar. 16, 2010) (rejecting theory that the flu vaccine causes different diseases

that have different direct antigens). For this reason alone, the Court should exclude their opinions on biological plausibility.

II. THERE IS NO RELIABLE EVIDENCE THAT PERINEALLY-APPLIED TALC CAN REACH THE FALLOPIAN TUBES OR OVARIES.

Plaintiffs' experts' biological plausibility opinions are also unreliable and inadmissible because they lack scientific support for any of the steps in the purported causal chain that they have identified, starting with their theory that talc can migrate from outside the body to the fallopian tubes and ovaries.

A dozen of plaintiffs' experts (many of whom lack any qualifications with respect to gynecology or female anatomy) assert that talc can migrate from the perineum into the vagina, up the female reproductive tract, against the flow of gravity and vaginal and cervical mucus, to the fallopian tubes and ovaries.[40]

---

[40] (*See, e.g.*, Saed Rep. at 11-12 ("The ability of talc particles to migrate through the genital tract to the distal fallopian tube and ovaries is well accepted"); Zelikoff Rep. at 12-14 ("Animal and human studies demonstrate that talcum powder products can migrate from the perineal region to the ovaries.") (emphasis omitted); Kane Rep. at 4, 14 ("Talcum powder products and their constituent minerals can reach the ovaries through migration up the genital tract from the perineum to the fallopian tubes and ovaries."); Wolf Rep. at 11 ("The migration of particles, including talc, asbestos and other constituents of talcum powder products, from the vagina to the upper genital tract (tubes and ovaries) is a key element in the mechanism by which talcum powder products cause ovarian cancer."); *see also* Smith Rep. at 16-17; Smith-Bindman Rep. at 35; Clarke-Pearson Rep. at 7-8; Moorman Rep. at 33; Plunkett Rep. at 27-38; McTiernan Rep. at 8, 58-63, 66; Carson Rep. at 7-8; Siemiatycki Rep. at 30; Singh Rep. at 18-19, 57.)

Plaintiffs' experts' opinions are generally premised on three types of data, none of which supplies a reliable basis for the conclusion that talc can migrate from the perineum to the fallopian tubes or ovaries. ***First***, plaintiffs' experts claim that their theory is supported by findings of talc particles in ovarian or ovarian-cancer tissue. But the studies they cite found talc both in the ovarian tissue of women who used talc perineally and those who did not, suggesting that the talc came from somewhere else – e.g., contamination or ingestion. ***Second***, plaintiffs' experts rely on the results of human and animal studies purportedly demonstrating that various non-talc particles are able to move through the reproductive tract. But these studies generally involved the insertion of particles (often other than talc) ***into the vagina***, used various methods to encourage upward movement, and – in most cases – did not demonstrate migration to the fallopian tubes or ovaries despite all of the artificial efforts made to facilitate migration.[41] ***Third***, while plaintiffs

[41] Many of plaintiffs' experts also rely on the statement by the FDA in a letter responding to a Citizen's Petition in 2014 that "the potential for particulates to migrate from the perineum and vagina to the peritoneal cavity is indisputable." (*E.g.*, Zelikoff Rep. at 13-14; Plunkett Rep. at 28; Moorman Rep. at 33; Singh Rep. at 19, 57; Wolf Rep. at 11 n.6.) But the FDA cited nothing in support of this conclusion, making it impossible to evaluate the basis for the FDA's statement. (*E.g.*, Dep. of Gregory B. Diette, M.D. 433:12-435:12, Apr. 9, 2019 (attached as Ex. B26 to Tersigni Cert.).) Plaintiffs' experts' reliance on this solitary sentence from the FDA letter is most notable because they seek to disregard the rest of the letter, which overwhelmingly disagrees with all of their other conclusions as to the Bradford Hill factors, including biological plausibility specifically, as to which the FDA concluded: "A cogent biological mechanism by which talc might lead to

(cont'd)

have largely abandoned the theory that talc can reach the ovaries though inhalation, several of their experts continue to offer this as a backup theory of transport. The scientific evidence cited by these experts undermines rather than supports the notion that inhaled talc moves through the lymphatic system to the ovaries or fallopian tubes.

A. Evidence Of Talc Particles In Human Reproductive Tissue Is Limited And Does Not Support The Hypothesis That Talc Applied Perineally Migrates To The Ovaries.

Nearly all of plaintiffs' experts who proffer opinions on talc migration rely on three studies in which researchers purported to identify talc particles in tissue taken from the reproductive tracts of human patients: Henderson (1971) (observing talc particles in the tissue of ten patients diagnosed with ovarian cancer and five patients with no ovarian cancer);[42] Cramer (2007) (case report of a single woman with ovarian cancer who was identified as having talc within a ***lymph***

(cont'd from previous page)
ovarian cancer is lacking." Letter from Steven M. Musser, Ph.D., Deputy Dir. for Sci. Operations, Ctr. for Food Safety & Applied Nutrition, to Samuel S. Epstein, M.D., Cancer Prev. Coalition, Univ. of Ill. – Chi. School of Pub. Health, at 4 (Apr. 1, 2014) (attached as Ex. A89 to Tersigni Cert.).

[42] Henderson et al., *Talc and Carcinoma of the Ovary and Cervix*, J Obstet Gynaecol Br Commonw. 266 (1971) ("Henderson 1971") (attached as Ex. A61 to Tersigni Cert.) (cited in Saed Rep. at 12; Smith-Bindman Rep. at 13, 35; Kane Rep. at 13-14; McTiernan Rep. at 58; Carson Rep. at 4; Clarke-Pearson Rep. at 8; Smith Rep. at 16; Wolf Rep. at 11; Plunkett Rep. at 33; Moorman Rep. at 33; Singh Rep. at 18, 57); *see also* Ness et al., *Factors Related to Inflammation of the Ovarian Epithelium and Risk of Ovarian Cancer*, 11(2) Epidemiol. 111 (2000) (attached as Ex. A106 to Tersigni Cert.).

node);[43] and Heller (1996) (detecting talc in the ovaries of 24 patients who underwent oophorectomies, including 12 who reported heavy cosmetic talc usage and 12 who reported none).[44]

---

[43] Cramer et al., *Presence of Talc in Pelvic Lymph Nodes of a Woman With Ovarian Cancer and Long-Term Genital Exposure to Cosmetic Talc*, 110(2) Obstet Gynecol 498 (2007) ("Cramer 2007") (attached as Ex. A24 to Tersigni Cert.) (cited in Saed Rep. at 12; Kane Rep. at 4, 14; McTiernan Rep. at 59; Wolf Rep. at 11; Plunkett Rep. at 29; Moorman Rep. at 33; Singh Rep. at 18, 57; Siemiatycki Rep. at 65; Zelikoff Rep. at 14).

[44] Heller 1996 – Talc at 1507 (cited in Smith-Bindman Rep. at 35; Kane Rep. at 14; McTiernan Rep. at 58, 59; Carson Rep. at 6; Clarke-Pearson Rep. at 8; Wolf Rep. at 11; Plunkett Rep. at 28, 29, 35; Moorman Rep. at 33; Singh Rep. at 57; Siemiatycki Rep. at 65; Zelikoff Rep. at 19). One additional study published after plaintiffs' experts issued their reports by another group of their litigation experts, McDonald and others, purports to "expand[] on the lymph node analysis" done in the Cramer 2007 case report by "examin[ing] the nodes in 22 patients with various types of ovarian tumors." McDonald et al., *Correlative polarizing light and scanning electron microscopy for the assessment of talc in pelvic region lymph nodes*, 43 Ultrastructural Pathol. 1, 2 (2019) ("McDonald 2019") (attached as Ex. A93 to Tersigni Cert.). The authors of that study claim that the "birefringent particles present within lymph nodes were taken to indicate clinically significant talc that migrated there through the lymphatic system." *Id.* at 3. As set forth below, plaintiffs have largely abandoned any lymphatic transport theory, presumably because there is no reason to believe particles would migrate ***out*** of the lymphatic system into organs like the ovaries. (*See* Part II.C.) In addition, given the authors' concession that some of the birefringent material is "likely nonspecific particulate material which finds its way into the perineum through general living and hygiene practices," McDonald 2019 at 13, it is not clear how many of the particles found in the lymph nodes were in fact talc. *See also id.* (concluding only that the birefringent material "is ***likely*** to be talc") (emphasis added). And in any event, because this study was limited to assessing the presence of talc in lymph nodes in the pelvic region, it provides ***no*** evidence that talc moved from the lymphatic system to the ovaries or fallopian tubes.

But the most that these publications show is that talc – from some source – can be found in human ovaries or lymph nodes. Not one of these studies comes anywhere close to concluding, as plaintiffs' experts contend, "that talcum powder applied to the perineum may be absorbed into the vagina and migrate . . . to the tubes and ovaries."[45]

To the contrary, Heller (1996) observed talc in the ovarian tissue of ***both*** women who used cosmetic talc ***and those who did not***, underscoring the speculative nature of plaintiffs' experts' assumption that the mere presence of talc particles in reproductive tissue means that it must have migrated up from the perineum.[46] Indeed, subsequent literature has explained that the Heller results may have reflected laboratory contamination.[47]

---

[45] (Smith-Bindman Rep. at 35; *see also* McTiernan Rep. at 59 (claiming these studies "demonstrate talcum powder products can migrate from the perineal area to the ovaries and fallopian tube").)

[46] (*See, e.g.*, Plunkett Rep. at 29 (misleadingly citing Heller for the proposition that talc can be found "in the ovaries of women who had reported use of talcum powder products," but ignoring the similar findings in women who had not); Carson Rep. at 8 (asserting that "[t]alc particles have been identified in reproductive system structures of women who utilize talc powders" but failing to mention that Heller also found talc in women without reported talc use); Zelikoff Rep. at 13 (citing Heller as "support[ing] the ability of talc to migrate from the perineal region upward and reach the upper genital tract" without mentioning that talc was found in the ovarian tissue of women with no reported perineal talc use).) Some of plaintiffs' experts also mention another study by Heller and colleagues that purported to find ***asbestos*** in the ovaries of some women undergoing oophorectomies. *See* Heller et al., *Asbestos Exposure and Ovarian Fiber Burden*, 29 Am. J. Indus. Med. 434 (1996) (attached as Ex. A59 to Tersigni Cert.) (cited in *(cont'd)*

Courts routinely exclude expert opinions where, as here, there is simply too great an analytical gap between the studies on which the experts rely and the conclusions that the experts draw from those studies. *See Heller v. Shaw Indus., Inc.*, 167 F.3d 146, 159 (3d Cir. 1999) (expert's testimony on causal relationship between carpet installation and plaintiff's illness was properly excluded because such a conclusion "did not reliably flow from th[e] data and methodology"); *Schepise v. Saturn Corp.*, No. CIV.A. 94-385(MLP), 1997 WL 897676, at *16-17 (D.N.J. July 30, 1997) (Wolfson, J.) (excluding expert who relied on studies that did not support her conclusions); *McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233, 1248 (11th Cir. 2005) (experts demonstrate a "lack of scientific rigor" when they draw "unauthorized conclusions from limited data—conclusions the authors of the study do not make"). Because studies finding talc in women's ovaries say absolutely nothing about how the talc got there (especially when many of the

---

(cont'd from previous page)
Smith-Bindman Rep. at 35, Clarke-Pearson Rep. at 8, Levy Rep. at 13). This study obviously has no bearing on whether ***talc*** can reach the ovaries or fallopian tubes, much less whether it can reach these organs as a result of normal perineal dusting.

[47] Notably, the McDonald article that plaintiffs' counsel have used at defendants' experts' depositions (*see* n.44, *supra*), which reported detecting talc in pelvic lymph nodes of both talc users and nonusers, expressly acknowledges that contamination is probably the best explanation for the Heller findings. McDonald 2019 at 7 tbl. 1, 12. Acknowledging Heller's findings, Dr. McTiernan speculates that the women who were not exposed to talc from perineal use must have inhaled talcum powder, but offers no support for her conjecture. (*See* McTiernan Rep. at 58.)

women in the studies had no history of perineal talc use), there is simply "'too great an analytical gap between the data and the opinion[s] proffered' [by plaintiffs' experts] to permit the testimony to be found reliable." *In re Mirena IUS Levonorgestrel-Related Prods. Liab. Litig. (No. II)*, 341 F. Supp. 3d 213, 271 (S.D.N.Y. 2018) (citation omitted).

B. None Of The Experimental Studies Cited By Plaintiffs Validates The Theory That Talc Travels From The Perineum To The Ovaries.

Several of plaintiffs' experts also assert that various experimental studies show that talc applied perineally can enter the vagina, travel through the cervix and endometrium and then travel up through the fallopian tube to the ovary.[48] But these opinions are not supported by science because the human studies on which they rely involved insertion of particles into the genital tract, frequently in environments manipulated to encourage the movement of those particles further up the genital tract, and many of them do not involve talc at all. Plaintiffs' experts also point to animal studies that either do not involve talc or involve talc exposure

[48] (*See, e.g.*, Zelikoff Rep. at 12-14; Carson Rep. at 7; Clarke-Pearson Rep. at 7-9; Kane Rep. at 4, 14; McTiernan Rep. at 8, 58; Moorman Rep. at 33; Plunkett Rep. at 28, 37; Singh Rep. at 18; Smith-Bindman Rep. at 5, 35; Wolf Rep. at 10; Saed Rep. at 12; Siemiatycki Rep. at 65; Smith Rep. at 16.)

in circumstances with no similarity to perineal talc use. Accordingly, these studies likewise fail to supply a reliable basis for plaintiffs' experts' migration opinions.[49]

1. Human Studies Do Not Support Plaintiffs' Experts' Migration Opinions.

The human studies cited by plaintiffs' experts do not support their migration theories because the majority of the studies do not involve talc and ***none observed the migration of particulates when applied in a manner resembling perineal dusting***. Indeed, many of the studies followed procedures that Egli & Newton, in the first such study performed, candidly described as "set[ting] up, as far as possible, conditions that were optimal for rapid transport" of the inserted particles.

First, although plaintiffs' experts baldly claim that "transport of talc-containing materials from the perineum . . . has been shown to occur with startling regularity,"[50] they do not cite a single human study involving application of any

---

[49] Plaintiffs' experts also fail to address anatomical differences that make the migration theory less plausible for women who have had few or no children. Specifically, Dr. Plunkett theorized that "wom[e]n who ha[ve] . . . had many children ha[ve] [genital] tract[s] that [are] stretched," allowing for "more direct contact than . . . with a very tight" genital tract. (Dep. of Laura Plunkett, Ph.D., D.A.B.T. 296:19-297:11, Dec. 19, 2018 (attached as Ex. B33 to Tersigni Cert.).) Of course, under this theory, whether talc can migrate to the ovaries "depends on the woman and . . . the situation." (*Id.*) Nevertheless, plaintiffs' experts indiscriminately contend that talc particles can migrate from the perineum to the ovaries as a general matter in all perineal talc users.

[50] (Carson Rep. at 7; *see also* Zelikoff Rep. at 14 ("Animal and human studies demonstrate that talcum powder products can migrate from the perineal region to the ovaries"); Clarke-Pearson Rep. at 9 ("Evidence shows that talcum powder *(cont'd)*

substance on the external perineum.[51] Rather, in ***every single one*** of the cited studies involving particle transport, particles were inserted well into the genital tract, and in the majority of these studies, particles were inserted at the posterior fornix, in the back of the vagina or near the cervical opening.[52] Sometimes, the

_____

(cont'd from previous page)

ascends from the perineum through the vagina, cervix and uterus into the fallopian tubes and onto the ovary."); Kane Rep. at 4 ("Talcum powder products and their constituent minerals can reach the ovaries through migration up the genital tract from the perineum to the fallopian tubes and ovaries."); McTiernan Rep. at 8 ("Published laboratory and clinical studies . . . have shown that in humans, talc can migrate from the perineum to the ovaries. . . ."); Moorman Rep. at 33 ("[T]alcum powder products can migrate from the perineum through the genital tract to the ovaries and fallopian tubes . . . ."); Plunkett Rep. at 37 (opining that animal and human studies "provide support for the FDA statement in 2014 that the potential for particulates to migrate from the perineum and vagina to the peritoneal cavity 'is indisputable'"); Smith-Bindman Rep. at 5 ("Observational and experimental data confirm that talcum powder product particles applied to the perineum can reach the fallopian tubes and ovaries through the vagina . . . ."); Wolf Rep. at 11 (opining that "perineal application resulting in migration and transport of particles through the genital tract" is a "recognized route of exposure").)

[51] Dr. Clarke-Pearson conceded that he could not name any study that traces externally applied talc through the reproductive tract to the ovaries, and instead argued that migration is possible simply because "the vagina is open to the outside world" and "there's no lid at the opening of the vagina." (Dep. of Daniel L. Clarke-Pearson, M.D. 88:23-90:9, Feb. 4, 2019 (attached as Ex. B10 to Tersigni Cert.).) Needless to say, this flippant remark does not substitute for reliable science.

[52] *See* Zervomanolakis et al., *Physiology of Upward Transport in the Human Female Genital Tract*, 1101 Ann. N.Y. Acad. Sci. 1, 3, 7 fig.1, 10 (2007) ("Zervomanolakis 2007") (attached as Ex. A159 to Tersigni Cert.) ("posterior vaginal fornix") (cited in Plunkett Rep. at 28, 36; Wolf Rep. at 11); Kadanali et al., *Evaluation of active and passive transport mechanisms in genital tracts of IUD-bearing women with radionuclide hysterosalpingoscintigraphy*, 63 Contraception 41, 42 (2001) ("Kadanali 2001") (attached as Ex. A83 to Tersigni Cert.) ("into the

(cont'd)

particles were deposited even further along the path toward the fallopian tubes and ovaries. For instance, De Boer (1972) placed particles either in the uterine cavity, cervical canal or vagina passage.[53] Moreover, De Boer found that passage to the fallopian tubes was only frequent for particles deposited ***in the cervical canal or***

(cont'd from previous page)
posterior vaginal fornix") (cited in Plunkett Rep. at 28, 36); Kunz et al., *The Uterine Peristaltic Pump: Normal and Impeded Sperm Transport within the Female Genital Tract*, *in* The Fate of the Male Germ Cell 267, 270 (Ivell & Holstein eds. 1997) ("Kunz 1997") (attached as Ex. A86 to Tersigni Cert.) ("at the external [orifice] of the uterine cervix") (cited in Plunkett Rep. at 28, 36; Wolf Rep. at 11; Saed Rep. at 12 & n.75); Iturralde & Venter, *Hysterosalpingo-Radionuclide Scintigraphy (HERS)*, 9(4) Seminars in Nuclear Med. 301, 304 (1981) ("Iturralde & Venter 1981") (attached as Ex. A80 to Tersigni Cert.) ("in the posterior fornix, or close to the cervical external [orifice]") (cited in Zelikoff Rep. at 12; Plunkett Rep. at 28); Venter & Iturralde, *Migration of a Particulate Radioactive Tracer from the Vagina to the Peritoneal Cavity and Ovaries*, SA Med. J. 917, 918 (1979) ("Venter & Iturralde 1979") (attached as Ex. A148 to Tersigni Cert.) ("deposited in the posterior fornix") (cited in Zelikoff Rep. at 12, 13-14; Carson Rep. at 7; Clarke-Pearson Rep. at 8; Kane Rep. at 14; McTiernan Rep. at 58 & n.88; Plunkett Rep. at 28, 31; Siemiatycki Rep. at 65; Wolf Rep. at 10-11); Egli & Newton, *The Transport of Carbon Particles in the Human Female Reproductive Tract*, 12 Fertility & Sterility 151, 152 (1961) ("Egli & Newton 1961") (attached as Ex. A31 to Tersigni Cert.) ("deposited in the posterior fornix") (cited in Zelikoff Rep. at 12-13; Carson Rep. at 7; Clarke-Pearson Rep. at 7-8; Kane Rep. at 14; McTiernan Rep. at 58 & n.85; Plunkett Rep. at 28, 29; Smith-Bindman Rep. at 35; Smith Rep. at 16; Wolf Rep. at 10). Several plaintiffs' experts cite the Kunz 1997 study to argue that uterine peristaltic contractions can foster the retrograde migration of inert particles such as talc. (*See* Plunkett Rep. at 35-36; Wolf Rep. at 11; Saed Rep. at 12 & n.75.) But as just noted, the Kunz study placed particles (albumin spheres, used as a proxy for sperm) directly into the reproductive tract, and accordingly fails to show that peristaltic contractions can aid the upward migration of perineally applied talc.

[53] De Boer, *Transport of Particulate Matter Through the Human Female Genital Tract*, 28 J Reprod Fert. 295 (1972) ("De Boer 1972") (attached as Ex. A26 to Tersigni Cert.) (cited in Plunkett Rep. at 28; Zelikoff Rep. at 12, 13).

the uterus, a finding at odds with plaintiffs' experts' conclusions that perineally applied talc could migrate so far. In Sjösten et al. (2004),[54] the particles were deposited from powdered gloves as part of a gynecologic examination, which typically involves the insertion of a speculum to open the vaginal vault and the insertion of one or two of the examiner's fingers into the vagina.[55]

Because the particles in these studies were inserted inside women's bodies rather than dusted on the outside, none of these studies provides any reliable support for the migration theory offered by plaintiffs' experts. For example, these studies neither account for gravity nor the possibility that the labia majora and labia minora prevent substances from entering the cervix and vagina.[56] Moreover, none of plaintiffs' experts addresses the differences between perineal dusting and physically inserting talc into the female reproductive tract. In short, none of the human studies relied on by plaintiffs' experts justifies an opinion that externally applied talc can migrate to the ovaries or fallopian tubes.

---

[54] Sjösten et al., *Retrograde migration of glove powder in human female genital tract*, 19 Hum. Reprod. 991, 992 (2004) (attached as Ex. A134 to Tersigni Cert.) (cited in Zelikoff Rep. at 12, 14; Carson Rep. at 7; Clarke-Pearson Rep. at 8; McTiernan Rep. at 59 & n.90; Moorman Rep. at 33 & n.150; Plunkett Rep. at 28, 36; Singh Rep. at 19 & n.68; Smith Rep. at 16; Wolf Rep. at 11).

[55] Bates et al., *The Challenging Pelvic Examination*, 26 J. Gen. Internal Med. 651 (2011) (attached as Ex. A10 to Tersigni Cert.); *see also* McTiernan Rep. at 59 (noting this study involved a "gloved hand inserted into the vagina").

[56] (*E.g.*, Dep. of Brooke T. Mossman, M.S., Ph.D. ("Mossman Dep.") 340:18-341:13, Apr. 8, 2019 (attached as Ex. B7 to Tersigni Cert.).)

Second, researchers in the studies cited by plaintiffs took one or more additional steps to increase the likelihood that the inserted particles would reach the upper reproductive tract. For instance:

- All of the human studies involved women either lying down or with intentionally elevated pelvises, contrary to the normal angle of a woman's body while standing and applying talcum powder.[57] To the extent that insertion deep into the internal genital tract had not already removed much of the effect of gravity, the body position in these studies further ensured that particles could migrate up the genital tract either with, or at the very least not against, gravity.

- In several studies, the women were given oxytocin, a drug that induces muscular contractions.[58] The studies themselves

---

[57] *See, e.g.*, Zervomanolakis 2007 at 3 ("with the patient in a supine position"); Kadanali 2001 at 42 ("with the patient in a supine gynecological examination position"); Iturralde & Venter 1981 at 303 ("supine gynecologic examination position with the buttocks slightly elevated"); Venter & Iturralde 1979 at 917 (the same); Egli & Newton 1961 at 152 ("lithotomy position with . . . head tilted downward at an angle of 15º"). Sjösten 2004 did not report the position of the women, but it can be assumed that they were in a typical gynecological examination position. And in many cases, the women maintained this position for a significant time after the particles had been inserted. *See* Kadanali 2001 at 42 ("The position of the patients was not changed" for two hours); Iturralde & Venter 1981 at 304 ("[t]he patient was kept in this position for the next" three hours); Venter & Iturralde 1979 at 918 ("The patient was kept in this position for about [two] hours.").

[58] *See* Zervomanolakis 2007 at 4; De Boer 1972 at 295, 298 (oxytocin is referred to by the brand name "Syntocinon"); Egli & Newton (1961). Oxytocin was administered during these studies because they were undertaken to research fertility and natural "oxytocin is released" within the body during and following intercourse. *See* Zervomanolakis 2007 at 15.

acknowledge that the drug likely plays a role in transporting sperm – or inert particles – upward to the tubes and ovaries.[59]

- In some studies, further steps were taken to impose a physical barrier forcing the inserted particles to remain in or migrate up the interior genital tract.[60] In a similar vein, the study by Sjösten et al. (2004) involved powder deposited through gynecological examination, where the examiner may introduce the particles with considerable force.

None of plaintiffs' experts acknowledges these artificial conditions or attempts to explain why it would be appropriate to extrapolate from these studies to perineal talc use despite the significantly different testing conditions. For this reason, too, the human studies on which plaintiffs' experts rely do not offer sound scientific footing for their opinions.

Third, all of the studies on which plaintiffs' experts rely involved particles other than talc, such as carbon or albumin micro- or macro-spheres.[61] None of these studies addressed how the size and properties of the particles studied

---

[59] *See* Egli & Newton 1961 at 154; Zervomanolakis 2007 at 1 ("[o]xytocin appears to play a critical role" in increasing "the transport of sperm into the oviduct.").

[60] *See, e.g.*, Iturralde & Venter 1981 at 304 (after insertion, "[t]he vulva was . . . covered with a sanitary towel and the legs pressed or crossed together"); Venter & Iturralde 1979 at 918 ("The vulva was covered with a sanitary towel and the legs were pressed together to prevent the [inserted solution] streaming from the vagina and thus lowering count levels.").

[61] *See, e.g.*, Zervomanolakis 2007 at 4 ("radiolabeled microspheres"); Sjösten 2004 (surgical glove starch powder, presumably cornstarch); Kadanali 2001; (radiolabeled albumin macrospheres); Kunz 1997 (same); Iturralde & Venter 1981 (radiolabeled albumin microspheres); Venter & Iturralde 1979 (same); De Boer 1972 (colloidal carbon solution); Egli & Newton 1961 (carbon particles).

compare to talc, and none of plaintiffs' experts explains why these studies are applicable to talc.[62] In fact, many of these studies were specifically designed to mimic the movement of sperm, rather than talc.[63]

An expert cannot depend on the effects or behaviors of one substance to support a conclusion about a different substance without showing some basis for treating the two similarly. *See generally Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997) (expert opinion should be excluded if "there is simply too great an analytical gap between the data and the opinion proffered"). For this reason, too,

---

[62] The studies involving radiolabeled albumin are especially inapplicable to talc, since the radioactive tracer can easily disassociate from the larger particle as the protein in the albumin breaks down and be found in tissue that the micro- or macro-sphere itself could never reach. (*See* Birrer Rep. at 7.)

[63] *See, e.g.*, Egli & Newton 1961; De Boer 1972; Venter & Iturralde 1979; Iturralde & Venter 1981. Certain plaintiffs' experts, including Dr. Clarke-Pearson, also purport to rely on statements in an undergraduate textbook suggesting that "sperm particles that would be non-motile" can "ascend from the vagina through the uterus and into the fallopian tube" as evidence that inert talc particles can do the same. (Clarke-Pearson Rep. at 7 (citing Jones & Lopez, *Gamete Transportation and Fertilization*, *in* Human Reproductive Biology 235 (3d ed. 2006) ("Jones & Lopez 2006")) (attached as Ex. A82 to Tersigni Cert.); *see also* Wolf Rep. at 10; Smith-Bindman Rep. at 35 & n.104.) But the textbook at issue only addressed movement of immotile sperm within the uterus – not up the vagina and to the ovaries or fallopian tubes. Jones & Lopez 2006 at 235. Moreover, the textbook explains that, to the extent non-motile sperm particles can travel through the uterus, they are driven by uterine "muscle contraction[s]" that result from high levels of oxytocin during and after intercourse, and their behavior cannot tell us anything about movement of inert particles through the uterus in other circumstances. *Id*. at 236. Thus, once again, the sources on which plaintiffs' experts rely do not support their ultimate conclusions.

none of the human experiments that plaintiffs' experts cite provides a reliable basis for their opinions.

2. Animal Studies Do Not Offer Reliable Proof Of Migration.

The animal studies relied on by a number of plaintiffs' experts – which explore the movement of particles in rats, rabbits or other animals – similarly cannot support their migration opinions, for several reasons. Indeed, some of plaintiffs' experts expressly acknowledge that the animal data fail to support the theory that talc can migrate from the perineum to the ovaries.[64] The other plaintiffs' experts who disagree with them lack a reliable basis for their opinions.

First, the animal studies related to migration have limited applicability to the question at hand because of major biological differences between rats and humans.

"[I]n order for animal studies to be admissible to prove causation in humans, there must be good grounds to extrapolate from animals to humans, just as the methodology of the studies must constitute good grounds to reach conclusions about the animals themselves." *In re Human Tissue Prods. Liab. Litig.*, 582 F. Supp. 2d 644, 657, 672-73 (D.N.J. 2008) (quoting *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 742-43 (3d Cir. 1994)) (excluding expert's opinion where he "failed to explain why it would be appropriate to extrapolate the results of this particular animal study to the human context" and "provided no explanation for his

64 (*See* Carson Rep. at 7; Singh Rep. at 18-19.)

ipse dixit leap from the identification of prions in bone marrow in animals to bone tissue in humans" because "the fact that one type of study is closer in model to a human model than another study does nothing more than prove that one or both studies may be inappropriate"); *Soldo*, 244 F. Supp. 2d at 547-48 (excluding causation opinions premised on animal studies because, *inter alia*, "plaintiff's experts did not demonstrate that the dog or the rat, i.e., the species in which these studies were performed, were sufficiently similar to a human being with regard to vasoconstrictive reactions to make reliance on such studies reasonable"). An expert's opinion applying animal studies to humans must therefore be based on an analysis of the "similarities and differences between the animal species in which the compound has been tested and humans."[65]

Here, none of plaintiffs' experts who rely on animal studies for their migration opinions analyzes the differences between the reproductive tracts of women and the animals that are the subjects of the studies. And the differences are manifold: among other things, all of the studies were performed on animals like rabbits and rodents that have much smaller reproductive tracts than humans.[66]

---

[65] Goldstein & Henifin, *Reference Guide on Toxicology*, *in Fed. Judicial Ctr.*, *Reference Manual on Scientific Evidence* 633, 661 (3d ed. 2011) (attached as Ex. A46 to Tersigni Cert.).

[66] (*See* Expert Report of Ie-Ming Shih, M.D., Ph.D. ("Shih Rep.") at 14, Feb. 25, 2019 (attached as Ex. C20 to Tersigni Cert.) (noting that "as compared to the murine genital tract, the human fallopian tube and ovary are 'far' away from the *(cont'd)*

Several of plaintiffs' own experts concede that the significant "differences between animals and humans in terms of anatomy of the genital tract" undermine the reliability of animal studies, but many of them continue to rely on those studies anyway.[67]

This fact alone is reason to exclude plaintiffs' migration theory opinions. *See Joiner*, 522 U.S. at 144-45 (affirming exclusion of expert opinions where experts relied on animal studies involving the exposure of high levels of PCBs to infant mice even though the adult humans' alleged exposure to PCBs was far less

---

(cont'd from previous page)
perineum").)

[67] (Plunkett Rep. at 29; *see also id.* at 31 ("studies in animals are not ideal in terms of modeling the female reproductive tract"); Zelikoff Rep. at 13 ("animal studies have limitations due to the differences in anatomy"); Carson Rep. at 7 (animal studies "are not as compelling as the human evidence because of anatomical and physiological differences between animals and humans").) As noted by the Health Canada Draft Screening Assessment, "Rodents are poor experimental models for perineal studies for a number of reasons. Ovulation in rodents occurs only or mainly during the breeding season, and rodent ovaries are variously enclosed in an ovarian bursa in comparison to human ovaries. Ovarian epithelial tumours are also rare in these animals. Ovarian tumours do occur in some strains of mice and rats; however, the low incidence and/or the length of time required for the appearance of tumours renders them poorly feasible for experimental studies of ovarian carcinogenesis." *See* Draft Screening Assessment at 15 (citations omitted); *see also* Cramer et al., *Genital Talc Exposure and Risk of Ovarian Cancer*, 81 Int'l J. Cancer 351, 356 (1999) (attached as Ex. A23 to Tersigni Cert.) ("Rodent models seem poorly suited to address these issues because of their infrequent ovulation and the fact that the rodent ovary is encased in a bursal sac."); Taher 2018 at 27 ("Rodent models may be of limited relevance because of ovulations occurring only or mainly during the breeding season and the rarity of ovarian epithelial tumors in these animals and ovaries are variously enclosed in an ovarian bursa.").

than the exposure in the animal studies; experts failed to "explain[] how and why the[y] could have extrapolated their opinions from these seemingly far-removed animal studies"). As courts have repeatedly recognized, experts must provide a "reasoned basis" for extrapolating from animal studies to conclusions about biological mechanism; such extrapolations cannot be drawn "uncritically" consistent with scientific principles. *Wade-Greaux v. Whitehall Labs., Inc.*, 874 F. Supp. 1441, 1482 (D.V.I. 1994) (excluding experts who relied on animal studies that bombarded chick embryos with abnormal dosages of a medicine to support opinion that the medicine was teratogenic in humans; the experts did not provide "any reasoned basis to bridge the analytical gap between experimental dosages in chick studies and therapeutic dosages in humans"), *aff'd*, 46 F.3d 1120 (table), 1994 WL 16973481 (3d Cir. 1994); *In re Rezulin Prods. Liab. Litig.*, 369 F. Supp. 2d 398, 407 (S.D.N.Y. 2005) ("[E]xtrapolation from animal studies to humans cannot be done uncritically. For one thing, different species have important physiological differences. For another, the high doses often used in animal studies may not correspond to considerably lower concentrations of a drug or other substance to which humans are in reality exposed."). Yet, that is precisely what plaintiffs' experts have done here, rendering their opinions unreliable.

Second, the most biologically relevant animal study – Wehner (1986) – undermines plaintiffs' migration hypothesis.[68] This study is particularly important because it is the *only* study to date that has examined the possible migration of talc, as opposed to other particles, and done so in primates, as opposed to rodents.[69] *See, e.g.*, *Bourne ex rel. Bourne v. E.I. Dupont de Nemours & Co.*, 189 F. Supp. 2d 482, 496 n.21 (S.D. W. Va. 2002) ("Primates are considered to render the most persuasive results with respect to extrapolation of the results to humans . . . ."). In Wehner's study, researchers vaginally deposited cosmetic talc into cynomolgus monkeys 30 times throughout a 45-day period. Two days after the last talc application, the authors examined tissue from the monkeys' ovaries, oviducts, uterus, vagina and cervix.[70] The authors found that only the vagina and cervix tissue samples – the organs in the area where the talc had been directly deposited –

---

68 Wehner et al., *On Talc Translocation From the Vagina to the Oviducts and Beyond*, 24 Food Chem Toxicol. 329 (1986) ("Wehner 1986") (attached as Ex. A149 to Tersigni Cert.) (cited in Plunkett Rep. at 33-34; Singh Rep. at 18, 57; Zelikoff Rep. at 13). Wehner and Weller's 1986 article was a follow up to determine whether a 1985 article following the same methodology and published in the same journal could "be reproduced in a larger number of animals."

69 Gardner et al. (1981) performed a monkey study, but used microcapsules hypothesized to function as a drug-delivery system, not talc. Gardner et al., *Potential Delivery of Contraceptive Agents to the Female Reproductive Tract*, *in* Controlled Release of Pesticides and Pharmaceuticals 99-109 (Lewis ed. 1981) ("Gardner 1981") (attached as Ex. A41 to Tersigni Cert.) (cited in Plunkett Rep. at 29, 34).

70 *Id.*

contained quantities of talc.[71] In other words, the study *found no translocation of talc to the oviducts*. This finding was in spite of the fact that the investigators took several steps to ensure that particles moved as far up the reproductive tract as possible: the animals were restrained with their pelvises 20 to 25 degrees above their bodies for at least 20 minutes, the talc suspension was deposited in the posterior fornix of the vagina (i.e., near the cervix) and the animals were treated with oxytocin to aid in particle transportation.[72] As a result, the authors concluded that talc could not migrate through the reproductive tract, noting that "the[] laws [of physics] would not permit particles to migrate 'upstream' against the direction of the beat of the oviduct's ciliary epithelium, even if the particles had managed to somehow breach the cervical barrier and diffuse across the uterine cavity."[73]

Many of plaintiffs' experts ignore the Wehner study altogether, demonstrating the sort of cherry-picking of favorable evidence that alone is reason to exclude their opinions. *See, e.g.*, *Zoloft*, 26 F. Supp. 3d at 461 (excluding expert who "fail[ed] to account for contrary evidence"). And those who do address the study fail to offer any reasoned basis to ignore its clear implications for their unsupported migration theories. For example, Drs. Plunkett and Singh note that

---

71 Wehner 1986 at 329, 331.

72 *Id.* at 337.

73 *Id.* at 338.

the study was funded by a cosmetic industry group, but they cannot point to any flaw in the methodology that might purportedly be traced to this apparently suspect funder.[74] Dr. Zelikoff attributes the findings to the study's "small sample size,"[75] but is happy to rely on other studies utilizing sample sizes in the same range, *e.g.*, Henderson, et al. (1986)[76] (eight rat pilot study and six treated-rat follow-up study); Ferrer (2002)[77] (study involving injection of high doses of talc into pleural cavities of 20 rabbits).[78] Thus, this is clearly not a methodologically valid basis for ignoring the conclusions of the Wehner study.

Third, the animal studies cited by plaintiffs' experts also do not help prove their migration theory because, much like the human studies discussed above, these

---

74 (*See* Plunkett Rep. at 34; Singh Rep. at 57.)

75 (Zelikoff Rep. at 13.)

76 Henderson et al., *The Demonstration of the Migration of Talc from the Vagina and Posterior Uterus to the Ovary in the Rat*, 40 Enviro. Res. 247 (1986) ("Henderson 1986") (attached as Ex. A62 to Tersigni Cert.) (cited in Zelikoff Rep. at 12-13; Siemiatycki Rep. at 65; Plunkett Rep. at 29, 33). Notably, Henderson and his colleagues were far more likely to find talc in the ovaries when it was deposited in the uterus than when it was deposited in the vagina.

77 Ferrer et al., *Influence of Particle Size on Extrapleural Talc Dissemination After Talc Slurry Pleurodesis*, 122(3) Chest 1018, 1019 (2002) ("Ferrer 2002") (attached as Ex. A36 to Tersigni Cert.).

78 Other plaintiffs' experts rely on animal studies with even smaller sample sizes. *See, e.g.*, Phillips et al., *Studies on the Absorption and Disposition of ^{3}H-Labelled Talc in the Rat, Mouse, Guinea-Pig and Rabbit*, 16 Toxicol. 161 (1978) ("Phillips 1978") (limited migration found in ***three*** intravaginally treated rabbits) (attached as Ex. A113 to Tersigni Cert.) (cited in Plunkett Rep. 29-30).

studies involved the introduction of particles into the animals' bodies and therefore do not replicate the external use of talc. In almost all of the studies cited, particles were inserted well into the internal reproductive tract, into the vagina or even into the uterus.[79] Moreover, in many of the studies, even if some migration was shown, talc did not reach the ovaries or fallopian tubes.[80]

The only animal study cited by plaintiffs' experts to support their migration opinions that involved external talc application was Keskin (2009), in which the study authors sprayed aerosolized talc on rats.[81] As explained below, this study ultimately concluded that talc *cannot* induce neoplastic change – a finding directly contrary to plaintiffs' theory of the case. Nevertheless, Dr. Zelikoff seizes on the fact that infection was found in some ovaries to infer talc migration.[82] But even if the talc in that study did make its way to the rats' ovaries, which is unclear, the

---

79 *See* Phillips 1978 at 162 ("single intravaginal dose" or "daily doses . . . intravaginally"); Gardner 1981 at 100, 103 ("insertion in the vagina" via "a . . . plunger"); Henderson 1986 at 247 ("intra-uterine installation of . . . talc suspension" in one experiment and "into the vagina[]" in another).

80 Phillips 1978 at 163 (after insertion of radioactively-labeled talc, "no radioactivity was found in the ovaries" and only very "small amount" past the vagina); Gardner 1981 at 99 (migration "***to the uterus***" (but no further) found in some monkeys and to the fallopian tubes of a single baboon) (emphasis added).

81 Keskin et al., *Does long-term talc exposure have a carcinogenic effect on the female genital system of rats? An experimental pilot study*, 280(6) Arch. Gynecol. Obstet. 925 (2009) ("Keskin 2009") (attached as Ex. A85 to Tersigni Cert.) (cited in Zelikoff Rep. at 13).

82 (*See* Zelikoff Rep. at 13.)

study involved sprayed aerosol talc, not sprinkling of talc dust, and the animals received doses of 400mg/kg of body weight – the equivalent of a 132-pound woman using well more than half a travel-sized bottle per day.[83] Thus, this study did not provide relevant information about the consequences of a woman dusting her perineum with talc.

In short, the animal studies on which plaintiffs' experts rely show, at most, that particles – sometimes talc and sometimes not – usually inserted well into the female reproductive tract, may be able to migrate a bit further. They *do not* provide reliable support for plaintiffs' theory that talc sprinkled on the external perineum can migrate the entire length of the reproductive tract and settle in the fallopian tubes or ovaries. *See, e.g.*, *Hollander v. Sandoz Pharm. Corp.*, 95 F. Supp. 2d 1230, 1238-39 (W.D. Okla. 2000) (excluding expert opinion that the drug Parlodel causes strokes in post-partum women in part because it was premised on expert's extrapolation from animal studies that involved very different circumstances of exposure), *aff'd in part and remanded on other grounds*, 289 F.3d 1193 (10th Cir. 2002).

---

[83] Keskin 2009 at 926 ("Talc with saline was given in aerosol form to the animals; dust form was not applied."). Another set of animals in the Keskin study received intravaginal talc application. *Id.*

C. There Is No Reliable Evidence That Perineally-Applied Talc Can Reach The Fallopian Tubes Or Ovaries Through Inhalation Or Lymphatic Transport.

Plaintiffs have largely abandoned the theory that talc reaches the ovaries through inhalation and lymphatic transport of talc particles. Indeed, most of plaintiffs' experts who discuss inhalation at all do so in a perfunctory manner, addressing it only as a potential "secondary route of exposure,"[84] or describing the inhalation theory as merely something that has been "hypothesiz[ed]."[85] To the extent plaintiffs continue to press this theory as a back-up to their migration hypothesis, it is entirely speculative and unreliable because: (1) there is no reliable science demonstrating that inhaled talc can be transported to the ovaries; and (2) the lack of any connection between talc inhalation and cancers of the lymphatic system or other organs significantly undermines the notion that inhaled talc travels through the body and causes systemic inflammation linked to cancer.

First, plaintiffs' inhalation/lymphatic transport theory is not supported by the published science. As plaintiffs' experts are forced to concede, IARC has expressly considered the issue of whether talc inhalation causes cancer and

---

[84] (Carson Rep. at 8; *see also* Smith Rep. at 19; Clarke-Pearson Rep. at 8; Kane Rep. at 14; Moorman Rep. at 33-34; Singh Rep. at 57-58; Wolf Rep. at 9, 11, 15; Plunkett Rep. at 28; McTiernan Rep. at 58.)

[85] (Siemiatycki Rep. at 65 ("In addition, as has been hypothesized and partially demonstrated in the discussion of asbestos and ovarian cancer, such particles might reach the ovaries via inhalation and translocation.").)

concluded that there is "insufficient evidence of carcinogenicity by the inhalation route."[86] In addition, several of plaintiffs' experts acknowledge that no published articles demonstrate that talc can be inhaled and then transported to the ovaries and cause inflammation there.[87]

Given this lack of relevant scientific support, plaintiffs' experts resort to pointing to irrelevant studies that do not support their opinions. For example, Dr. Zelikoff's report offers what is perhaps the most full-throated endorsement of the inhalation theory. But she relies largely on irrelevant studies involving the ***direct injection or installation of substances (not always talc) in rats and other animals***.[88] Dr. McTiernan also speculates that Heller's pathological findings of

---

86 (Carson Rep. at 4.)

87 (Dep. of Patricia G. Moorman, M.S.P.H., Ph.D. 303:17-304:14, Jan. 25, 2019 (attached as Ex. B39 to Tersigni Cert.); Dep. of Sonal Singh, M.D., M.P.H. ("Singh Dep.") 216:14-19, Jan. 16, 2019 (attached as Ex. B47 to Tersigni Cert.); *see also* Expert Report Of Brooke Taylor Mossman, M.D., Ph.D. at 37, Feb. 25, 2019 (attached as Ex. C11 to Tersigni Cert.) (explaining that "there are no peer-reviewed studies demonstrating that inhaled talc causes inflammation in the ovaries").)

88 (*See* Zelikoff Rep. at 14-15 (citing Driscoll et al., *Effects of particle exposure and particle-elicited inflammatory cells on mutation in rat alveolar epithelial cells*, 18(2) Carcinogenesis 423 (1997)) (reporting effect of intratracheal installation of quartz, carbon black and titanium dioxide in rats on cells in lungs); Werebe et al., *Systemic Distribution of Talc After Intrapleural Administration in Rats*, 115(1) Chest 190, 191 (1999) (attached as Ex. A150 to Tersigni Cert.) (particles observed in the chest wall, lungs, heart, brain, spleen and kidneys of rats directly injected with high doses of talc slurry); Ferrer 2002 (reporting on the injection of high doses of two different sizes of talc into the pleural cavities of 20

(cont'd)

talc in the ovarian tissue of women with no reported perineal talc use "suggests additional routes of exposure to talc, such as inhaled powder," but she provides no scientific support for this assertion.[89]

Other experts addressing inhalation rely on similarly irrelevant studies that address findings of asbestos and/or involve non-reproductive organs – ***not*** talc or the fallopian tubes/ovaries – and therefore do nothing to prove that inhaled talc can migrate there through the lymphatic system. For example, Drs. Kane, Plunkett and Singh cite to a study documenting the finding of asbestos fibers in the lungs, pleural tissue and peritoneal tissue of occupationally exposed men.[90] These same experts also point to studies examining the consequences of asbestos or talc exposure on the lungs.[91] In addition, Dr. Plunkett relies extensively on a series of

(cont'd from previous page)
rabbits, after which the authors observed particles in the lungs, chest wall, diaphragm, mediastinal pleura, heart, liver, spleen and right kidney); Genofre et al., *Talc Pleurodesis: Evidence of Systemic Inflammatory Response to Small Size Talc Particles*, 103 Respiratory Med. 91 (2009) ("Genofre 2009") (attached as Ex. A44 to Tersigni Cert.) (involving direct injection of high doses of two different sizes of talc particles into the pleural cavities of 30 rabbits; no findings related to the reproductive system).)

89 (*See* McTiernan Rep. at 58.)

90 (*See* Kane Rep. at 14 (citing Suzuki & Kohyama, *Translocation of Inhaled Asbestos Fibers From the Lung to Other Tissues*, 19(6) Am J Indus Med. 701 (1991)); Singh Rep. at 57-58 (citing same article); Plunkett Rep. at 28 (citing same article).)

91 (*See* Singh Rep. at 57-58 (citing Bunderson-Schelvan et al., *Nonpulmonary Outcomes of Asbestos Exposure*, 14 J. of Toxicology and Envtl. Health Pt. B, 122-
(cont'd)

studies that purportedly identified lung lesions in rats and mice after the inhalation of talc.[92] But even Dr. Plunkett appears to concede that such studies – which did not observe ovarian tumors in the subjects – undermine plaintiffs' experts' inhalation theory. As Dr. Plunkett herself states, "the studies would not be expected to produce ovarian tumors in rats or mice given the [inhalation] route of exposure that would severely limit any perineal exposure to talc."[93]

Still other experts cite to Cramer's 2007 case report of a single patient with ovarian cancer, a history of talc use and the identification of talc within a lymph node.[94] As set forth above, however, talc was not found in the patient's ovarian or fallopian tube tissues, and the presence of talc in the lymph nodes has no known scientific relevance to the development of ovarian cancer.[95] Accordingly, none of

---

(cont'd from previous page)
52 (2011)); Plunkett Rep. at 28 (citing same article); Kane Rep. at 14 (citing Marchiori et al., *Pulmonary Talcosis: Imaging Findings*, 188(2) Lung 165 (2010) and Frank, *An Uncommon Hazard: Pulmonary Talcosis as a Result of Recurrent Aspiration of Baby Powder*, 4(3) Respiratory Med. CME 109 (2011)).)

92 (*See* Plunkett Rep. at 41 (citing Nat'l Toxicology Program, U.S. Dep't of Health & Human Servs., No. 453, *Toxicology and Carcinogenesis of Nickel Subsulfide (CAS No. 12035-72-2) in F344/N Rats and B6C3F1 Mice (Inhalation Studies)* (1996)).)

93 (*Id*.)

94 (*See, e.g.*, McTiernan Rep. at 59; Kane Rep. at 14; Wolf Rep. at 11; Singh Rep. at 18.)

95 (Birrer Rep. at 5-6.) Notably, the Cramer 2007 report disclaimed a causal conclusion, acknowledging that "case reports cannot establish causality" and that further research would be needed to substantiate causation. Cramer 2007 at 500.

these attenuated studies can support the conclusion that inhaled talc travels to the ovaries or fallopian tubes through the lymphatic system. *See, e.g.*, *Schepise*, 1997 WL 897676, at *17 (rejecting as unreliable expert causation opinions not directly supported by "studies, articles or any other medical authorities"; expert's reliance on tangentially-related science involving "different exposure in entirely different settings . . . cannot support her hypothesis"); *Ruggiero v. Warner-Lambert Co.*, 424 F.3d 249, 253 (2d Cir. 2005) ("[W]hen an expert opinion is based on data, a methodology, or studies that are simply inadequate to support the conclusions reached, *Daubert* and Rule 702 mandate the exclusion of that unreliable opinion testimony.") (quoting *Amorgianos v. Nat'l R.R. Passenger Corp.*, 303 F.3d 256, 266 (2d Cir. 2002)).

Second, plaintiffs' inhalation theory is significantly undermined by the fact that talcum powder use is not associated with any other cancers in organs more proximate to the respiratory system. Assuming that plaintiffs' experts' inhalation or lymphatic transport hypotheses were correct and talc could transport through the lymphatic system and cause cancer in the ovaries through chronic inflammation, it would follow that talc would also travel to different organs and cause cancer there, or at the very least be associated with lymphoma.[96] Indeed, Dr. Zelikoff herself testified that if talc could transport through the lymphatic system, then it should

[96] (*See* Kurman Rep. at 23.)

cause chronic inflammation – which she claims causes cancer – "systematically" through the body.[97] Yet, there are no studies or reports of any association of talcum powder with lymphoma or other cancers, rendering plaintiffs' experts' inhalation theory implausible.[98] *See In re TMI Litig.*, 193 F.3d 613, 683, 703 n.144 (3d Cir. 1999) (excluding expert opinion that residents in the area of a nuclear reactor accident were exposed to a dose of radiation known to be "lethal" because no radiation-related fatalities were reported following the accident and therefore the expert's dose opinion "fl[ies] in the face of reality"), *amended in nonmaterial part*, 199 F.3d 158 (3d Cir. 2000). In short, the backup inhalation theory advanced by some of plaintiffs' experts fails to meet any indicia of reliability and amounts to rank speculation. *See Soldo*, 244 F. Supp. 2d at 563 (refusing to admit "opinion evidence that is connected to existing data only by the *ipse dixit* of the expert" because a court "is not required to simply take the expert's word for it"). For these

---

97 (Zelikoff Dep. 306:2-307:1.)

98 (*See* Shih Rep. at 8 ("If talc particles can travel through the lymphatic channel to the ovaries, they should be able to reach other human body parts and tissues as well because the lymphatic system runs throughout the body," but there "are no reports showing that talc is associated with other types of female (or male) cancer like colon cancer, liver cancer, stomach cancer, prostate cancer and pancreatic cancer (where lymphatic circulation is active)"); *id*. at 9 (explaining that if talc particles "are carcinogenic, their presence in the lymph nodes (where the lymphatic drainage occurs) should lead to cancer in the lymph nodes (i.e., lymphoma), and there is no evidence of such a relationship").)

reasons, too, plaintiffs' experts' biological plausibility opinions do not satisfy the fundamental requirements of *Daubert*.

III. THERE IS NO RELIABLE EVIDENCE ESTABLISHING A PLAUSIBLE MECHANISM BY WHICH TALC COULD CAUSE OVARIAN CANCER EVEN IF IT REACHED THE FALLOPIAN TUBES OR OVARIES.

Even if it were plausible that trace amounts of asbestos or talc reach the ovaries or fallopian tubes after perineal dusting with cosmetic talc, plaintiffs' experts have failed to reliably pinpoint the mechanism by which talc could cause any subtype of ovarian cancer once there. Various plaintiffs' experts – including Drs. Saed, Zelikoff and others – assert that biological plausibility is satisfied because talc causes chronic inflammation in ovarian tissue, which then leads to ovarian cancer.[99] Plaintiffs' experts have also suggested, as an alternative theory, that the presence of talc in the body lowers a patient's production of Mucin 1 ("MUC1") antibodies, which in turn increases the risk of ovarian cancer.[100] But

---

[99] (*See, e.g.*, Saed Rep. at 20 ("[Talc] elicits an inflammatory response . . . that can result in the development and the progression of ovarian cancer."); Zelikoff Rep. at 26; Kane Rep. at 4; Moorman Rep. at 39-40; Levy Rep. at 11-13; Carson Rep. at 7; Clarke-Pearson Rep. at 4, 9; McTiernan Rep. at 62-63; Plunkett Rep. at 46; Siemiatycki Rep. at 65; Singh Rep. at 58-59, 65; Smith-Bindman Rep. at 12-13; Smith Rep. at 17-18; Wolf Rep. at 11-13.)

[100] (*See, e.g.*, Singh Rep. at 59 ("Some have suggested that perineal talc use may also increase risk of ovarian cancer by the induction of anti-MUC1 . . ., although the data are not definitive.") (endnote omitted); Saed Rep. at 12 ("It has been suggested that the associations between perineal talc dusting and ovarian cancer might be explained by the induction of ANTI-MUC1 antibodies.") (endnote

(cont'd)

these are merely ***hypotheses*** that have never been substantiated by the relevant published literature.[101] To the contrary, the science on these issues is, at best, unresolved – and, in some cases, significantly undermines plaintiffs' experts' biological plausibility theories. *See Henricksen*, 605 F. Supp. 2d at 1176 (rejecting expert causation opinions for lack of biological plausibility where the relevant studies "make clear that the connection" between the substance and disease at issue "is at this point in time only a hypothesis in need of further investigation"); *In re Accutane*, 511 F. Supp. 2d at 1296 ("If medical science does not know the cause [of the injury at issue], then (the expert's) 'theory' of causation" constitutes "conjecture, not deduction from scientifically-validated information").

A. Plaintiffs' Chronic Inflammation Theory Of Causation Is Scientifically Unsupported And Unreliable.

Plaintiffs' experts' opinions that talcum powder causes chronic inflammation, which, in turn, increases the risk of unspecified subtypes of ovarian cancer, are not the product of reliable methods and are contrary to established scientific knowledge. The biological plausibility of this hypothesis depends on two separate precepts: (1) that perineal talc use causes chronic inflammation; and

(cont'd from previous page)
omitted); Zelikoff Rep. at 19; Kane Rep. at 13.)

[101] (*See* Zelikoff Dep. 157:9-16 (not aware of "any medical or scientific community that has accepted that there is biologic plausibility of talcum powder products causing ovarian cancer").)

(2) that chronic inflammation is a factor in the development of some (or perhaps all) subtypes of ovarian cancer.[102] As set forth below, plaintiffs' experts lack reliable scientific evidence to support either proposition.

1. There Is No Scientific Support For The Proposition That Perineal Talc Use Causes Chronic Inflammation.

Plaintiffs' experts' hypotheses that perineal talc exposure causes chronic inflammation in the fallopian tubes or ovaries are scientifically unsupported. As Dr. Zelikoff notes, there are two types of inflammation: acute and chronic.[103] While "[a]cute inflammation . . . frequently precedes the development of protective adaptive immune responses to pathogens and cancer," chronic inflammation can contribute to the development of ***some*** tumors.[104]

The threshold problem with this theory is that there is a "lack of cogent evidence that talc deposits in humans are associated with chronic inflammation in normal fallopian tubes and ovaries."[105] Notably, Dr. Zelikoff herself admitted at

---

[102] (*See* Zelikoff Dep. 216:23-217:4 (noting the two-step process in establishing the biological plausibility of plaintiffs' inflammation theory).)

[103] (Zelikoff Rep. at 20.)

[104] (*Id.*)

[105] (Shih Rep. at 14; *see also* Neel Rep. at 20 ("There simply is no compelling evidence that talc induces an inflammatory response in the female genital tract.").)

deposition that she is not aware of any peer-reviewed literature reporting chronic inflammation in the genitourinary tract of women who report perineal talc use.[106]

Indeed, the small body of relevant research is to the contrary. Heller's 1996 study found ***no evidence*** of response to talc particles, such as foreign body giant cell reaction or fibrosis, in human ovarian tissue containing talc particles.[107] Similarly, the Henderson (1971) article – upon which many of plaintiffs' experts rely[108] – reported that ***no inflammation*** was present in the tissues where talc particles were purportedly found.[109] Consistent with these findings, Dr. Robert Kurman, a renowned gynecological pathologist, has "examined a number of surgical pathology specimens from plaintiffs in talc litigation and ha[s] not observed foreign body granulomas or foreign body granulomatous inflammation associated with alleged talc use."[110]

Ignoring this science, plaintiffs' experts point to a variety of animal studies that they claim support the hypothesis that perineal talc exposure causes chronic

---

106 (Zelikoff Dep. 356:13-358:4.)

107 *See* Heller 1996 – Talc.

108 (McTiernan Rep. at 58; Carson Rep. at 4; Clarke-Pearson Rep. at 8; Smith Rep. at 16; Saed Rep. at 12; Wolf Rep. at 5, 11; Plunkett Rep. at 26, 33, 49, 60; Moorman Rep. at 33; Smith-Bindman Rep. at 13, 35; Kane Rep. at 13-4, 16; Singh Rep. at 18, 57.)

109 *See* Henderson 1971.

110 (Kurman Rep. at 16.)

inflammation capable of causing cancer – but none shows such a causal relationship. For example, several experts rely on Keskin (2009), which (as discussed above) involved the application of aerosolized talc to rats, to support their inflammation opinions.[111] But in that study, the researchers merely observed infection and acute granulomas in animal groups exposed to talc – ***with no chronic inflammation or neoplastic changes observed in the tissue***.[112] Similarly, the Hamilton (1984) study,[113] which involved the injection of high concentrations of talc directly into the rat ovarian bursa, noted no evidence of inflammation. Although foreign body granulomas were seen, granulomas generally are not observed during human ovarian cancer development (e.g., in patients' precursor lesions for HGSOC)[114] and no malignancies were observed in the rat tissue

---

111 *See* Keskin 2009 (cited in McTiernan Rep. at 60; Moorman Rep. at 34; Wolf Rep. at 12; Zelikoff Rep. at 25).

112 *Id*. (*See also* Neel Rep. at 21 (authors of the Keskin study "observed foreign body reactions (granulomas), as well as infections, in both groups exposed to talc, but no neoplastic changes. [The authors] concluded that talc causes foreign body reaction and infection, but not cancer.").) Plaintiffs are unable to point to any data suggesting that perineal talcum powder use induces genital infection in the ***human*** body. (*See* Shih Rep. at 14.)

113 Hamilton et al., *Effects of Talc on the Rat Ovary*, 65(1) Br J Exp Pathol. 101 (1984) (attached as Ex. A53 to Tersigni Cert.) (cited in McTiernan Rep. at 62; Wolf Rep. at 12; Plunkett Rep. at 26, 39; Levy Rep. at 14; Singh Rep. at 59).

114 (*See* Kurman Rep. at 16 ("[I]n the course of my 40 years of looking at microscopic slides of ovarian cancer, I have only seen foreign body granulomatous inflammation associated with ovarian tumors very rarely. The associated tumors have been predominantly teratomas (which are not epithelial carcinomas); less than

(cont'd)

exposed to talc.[115] In short, the animal studies at issue fail to support the hypothesis that talc can cause chronic inflammation in ovarian tissue.

Other studies cited by plaintiffs' experts for the proposition that talc causes chronic inflammation capable of increasing the risk of cancer similarly do not support that point. For example, Dr. Kane asserts that "there are experimental studies in the literature that support a causal relationship between talc and ovarian cancer" by showing "increases in inflammatory markers following talc exposure."[116] But the studies cited by Dr. Kane do not show inflammation in ovarian tissue. Instead, Allaire (1989)[117] is a study of talc in liver tissue from IV drug users, while Genofre (2009)[118] and Arellano-Orden (2013)[119] are studies of

---

(cont'd from previous page)
a handful were endometrioid carcinomas. In all these cases, the granulomatous inflammation was in response to keratin produced by the tumor and had nothing to do with talc (no evidence of polarized crystals that may have been talc).").)

115 (Neel Rep. at 21; *see also* Birrer Rep. at 16-17.)

116 (Kane Rep. at 12.)

117 Allaire et al., *Talc in Liver Tissue of Intravenous Drug Abusers with Chronic Hepatitis*, 92(5) A.J.C.P. 583 (1989) (attached as Ex. A7 to Tersigni Cert.) (cited in Kane Rep. at 12, 36).

118 Genofre 2009 (cited in McTiernan Rep. at 60; Zelikoff Rep. at 16, 26; Kane Rep. at 36).

119 Orden et al., *Small Particle-Size Talc Is Associated with Poor Outcome and Increased Inflammation in Thoracoscopic Pleurodesis*, 86 Respiration 201 (2013) (attached as Ex. A108 to Tersigni Cert.) (cited in McTiernan Rep. at 60; Plunkett Rep. at 48; Kane Rep. at 12, 36).

pleurodesis, a beneficial procedure that has not been reported to cause cancer and involves a part of the body that is unrelated to ovarian carcinogenesis.[120]

Finally, Dr. Saed relies on Langseth & Kjaerheim, *Ovarian cancer and occupational exposure among pulp and paper employees in Norway*, 30(5) Scand. J. Work Envtl. Health 356 (2004) (attached as Ex. A87 to Tersigni Cert.) (cited in Saed Rep. at 10-11), as a supposed example of animal testing that demonstrated an association between talc and tumor formation or inflammation, but that article looked at ovarian cancers in Norwegian pulp and paper workers exposed to asbestos, talc or both dusts. It did not involve animals or study inflammation by pathology or other measures. Further, the authors expressly stated that "[t]he results do not confirm an association between exposure to asbestos, talc, and total dust and ovarian cancer."[121]

In short, plaintiffs' experts again premise their opinions on studies that do not actually support their conclusion – i.e., that talc can cause chronic inflammation in humans. For this reason, too, their methodologies are flawed and

---

120 Plaintiffs' experts fail to explain how their inflammation theory can be correct if large amounts of talc injected into the lungs during pleurodesis do not induce cancer. (Kurman Rep. at 19-20; *see also* Neel Rep. at 28 (noting that "humans given high doses of talc in other body cavities (e.g., via pleurodesis) . . . ***do not have increased cancer risk***," but "most of the pro-oncogenic mechanisms proposed by plaintiffs' experts would be expected to operate in multiple body sites") (emphasis added).)

121 *Id.* at 356 (abstract).

their opinions about biological plausibility should be excluded under *Daubert*. *See Zoloft*, 26 F. Supp. 3d at 462 (excluding expert's opinion because the studies the expert relied upon "do not adequately support her opinions").[122]

2. Plaintiffs' Experts Cannot Reliably Link Chronic Inflammation To Ovarian Cancer.

Plaintiffs' experts' theory of biological plausibility is also scientifically unreliable because their experts offer nothing other than unsubstantiated hypotheses and vague generalities to support the conclusion that chronic inflammation could cause any subtype of ovarian cancer (much less many or all of them). *See Schepise*, 1997 WL 897676, at *16-17 (excluding expert whose "only support . . . for her conclusions is the piece-meal compilation of a series of unrelated documents and articles"); *In re Accutane*, 511 F. Supp. 2d at 1296 (rejecting expert's theory of biological plausibility because it had "not been

[122] Plaintiffs' experts also fail to explain why talc would cause inflammation in the ovary but not in other intermediate tissues – such as the vagina, fallopian tube, cervix and endometrium – that are along the alleged path that talc would take from the perineum to the ovaries under plaintiffs' migration theory. Plaintiffs' experts' inability to explain critical facts that contradict the purported mechanism by which talc allegedly causes ovarian cancer severely undermines the reliability and "fit" of their causation testimony. *See Mause v. Glob. Household Brands, Inc.*, No. CIV.A. 01-4313, 2003 WL 22416000, at *3 (E.D. Pa. Oct. 20, 2003) (excluding expert's causation testimony that X-14 caused plaintiff's injuries for lack of fit because the expert "could not explain why there was an absence of irritation in the plaintiff's nose or mouth," how the product got to plaintiff's lungs, and other facts that undermined his causation theory).

verified by testing" or "peer reviewed" and therefore amounted to nothing more than "an educated guess").

The theory that inflammation can trigger ovarian cancer was first proposed as a "novel hypothesis" in a review article published in 1999, which concluded – based on much of the same literature plaintiffs' experts rely on here – that "[f]urther observational and experimental data [were] needed to confirm the hypothesis."[123] Two decades later, this hypothesis remains unproven – and recent evidence has refuted it, rather than supported it.[124]

---

[123] Ness & Cottreau, *Review: Possible Role of Ovarian Epithelial Inflammation in Ovarian Cancer*, 91(17) J. Nat'l Cancer Inst. 1459, 1459, 1464 (1999) (attached as Ex. A105 to Tersigni Cert.).

[124] The fact that several of plaintiffs' experts rely on the language from the Ness article to support their biological plausibility opinions highlights the speculative nature of their conclusions. (*See* Singh Rep. at 58 (citing only this study in arguing that "[i]nflammation has long been understood to be an important mechanism underlying the development of ovarian cancer"); *see also* Kane Rep. at 10; Siemiatycki Rep. at 65.) Plaintiffs and some of their experts also rely on similarly excerpted language from various epidemiological studies that speculate or hypothesize about a biological mechanism. (*See, e.g.*, Biologic Plausibility: Chronic Inflammation (Mossman Dep. Ex. 24) (attached as Ex. B8 to Tersigni Cert.).) But epidemiological studies are not designed to (and cannot) demonstrate a biological mechanism. And even the cherry-picked language from these articles is either speculative in nature or frankly admits that the biological mechanism by which talc would cause ovarian cancer is unknown or unproven. For instance, plaintiffs' experts cite another article by Ness and colleagues that refers to "the ***hypothesis*** that inflammation may mediate ovarian cancer risk" and notes that their data do "not completely" support the hypothesis. Ness et al., *Factors Related to Inflammation of the Ovarian Epithelium and Risk of Ovarian Cancer*, 11 Epidemiology 111, 111, 115 (2000) (attached as Ex. A106 to Tersigni Cert.) (emphasis added) (cited in Levy Rep. at 12, Kane Rep. at 10, 12, Siemiatycki Rep. *(cont'd)*

First, the studies that have evaluated markers of chronic inflammation for possible correlations with ovarian cancer (either in general or as to specific subtypes) have been inconclusive or, if anything, have suggested that there is no relationship. Most notably, a recent study by Malmberg tends to disprove a causal relationship between chronic inflammation and serous ovarian cancer.[125] That study involved the review of histological slides for markers of inflammation in tissue taken from three cohorts of women, including a group of women with hereditary risk of ovarian cancer, a group that had experienced ovarian cancer without hereditary risk and a control group.[126] Although the authors found increased inflammation between the cancer group and the control group, they specifically noted that it was "not significant."[127] The authors also explained that age could have been a confounder because "[c]learly, age could affect

---

(cont'd from previous page)
at 65, Singh Rep. at 37, 57-58). Similarly, several of plaintiffs' experts cite a paper by Gates and colleagues that focused on the association between ovarian cancer, talc use, and certain genetic variations, and speculated about a biological mechanism in passing. *See* Gates et al., *Talc Use, Variants of the GTSM1, GSTT1, and NAT2 Genes, and Risk of Epithelial Ovarian Cancer*, 17(9) Cancer Epidemiol Biomarkers Prev. 2436 (2008) (attached as Ex. A43 to Tersigni Cert.) (cited in Zelikoff Rep. at 26, Levy Rep. at 14, Kane Rep. at 35, Smith Rep. at 17).

125 *See* Malmberg et al., *Serous tubal intraepithelial carcinoma, chronic fallopian tube injury, and serous carcinoma development*, 468 Virchows Arch. 707 (2016) (attached as Ex. A91 to Tersigni Cert.).

126 *Id*. at 707 (abstract).

127 *Id*. at 712.

inflammation," and the mean age of women with cancer was four years higher than the women in the control group.[128] Accordingly, the authors concluded that "***no significant correlation was made between serous carcinoma and histological signs of inflammation***," and that more research would be necessary to "evaluate the role of inflammation in carcinogenesis in the fallopian tube."[129]

The scientific literature cited by plaintiffs' experts does not show otherwise. For instance, a number of plaintiffs' experts rely on Trabert et al. (2014),[130] which investigated 46 inflammatory serum markers for possible association with ovarian cancer generally and serous subtypes specifically.[131] Of the 46 markers studied, only two – C-reactive protein (CrP) and Interleukin (IL-)-1α – were associated with the risk of developing ovarian cancer (both ovarian cancer overall and serous

---

128 *Id.*

129 *Id*. (emphasis added). Similarly, Dr. Shih, the Richard W. TeLinde Distinguished Professor of Gynecological Pathology at the Johns Hopkins University School of Medicine, found inflammation in HGSOC tissue but not in its precursor lesions, giving rise to the inescapable inference that HGSOC causes inflammation, rather than the other way around. According to Dr. Shih, "the claim that talc deposition causes chronic inflammation, which subsequently causes ovarian cancer, is unsustainable." (Shih Rep. at 15.)

130 Trabert et al., *Pre-Diagnostic Serum Levels of Inflammation Markers and Risk of Ovarian Cancer in the Prostate, Lung, Colorectal and Ovarian Cancer (PLCO) Screening Trial*, 135 Gynecol Oncol. 297 (2014) ("Trabert 2014 – Serum") (attached as Ex. A143 to Tersigni Cert.)

131 (*See, e.g.*, Kane Rep. at 12; Clarke-Pearson Rep. at 4; Smith Rep. at 17; Zelikoff Rep. at 24; Plunkett Rep. at 46; Smith-Bindman Rep. (reliance list); Carson Rep. (reliance list); Kessler Rep. (reliance list); Wolf Rep. (reliance list); Moorman Rep. (reliance list); Singh Rep. (reliance list).)

subtypes specifically). As the authors of the study acknowledged, however, the measurements only reported ***systemic*** levels of inflammation and therefore "may not reflect levels in local sites of inflammation relevant to ovarian carcinogenesis," including "the fallopian tube, ovary or endometriotic lesions."[132] As a result, "the implications of the findings" by Trabert "are unclear and do not substantiate a link between local inflammation and ovarian cancer."[133]

A number of plaintiffs' experts also rely heavily on a 2007 study by Buz'Zard, et al. for the proposition that a link exists between inflammation and unspecified subtypes of ovarian cancer.[134] In that study, the authors purported to observe the effects of talc on various types of human cells and asserted that talc increased cell viability (cell number) at low doses, but decreased it at higher doses.[135] The study, however, is plagued by a host of methodological problems, including the fact that the underlying data do not support the conclusions that the

---

132 Trabert 2014 – Serum at 303.

133 (Birrer Rep. at 19; *see also* Neel Rep. at 24 (explaining that "there simply is no evidence . . . that links perineal talc exposure to inflammation" in Trabert and it "remains possible that increased CRP is a sign of inflammation that results from, rather than causes, ovarian cancer").)

134 *See* Buz'Zard & Lau 2007 (referenced in McTiernan Rep. at 60; Carson Rep. at 6; Clarke-Pearson Rep. at 4; Smith Rep. at 17, 21; Siemiatycki Rep. at 65; Wolf Rep. at 12; Zelikoff Rep. at 25; Plunkett Rep. at 26, 42, 50; Kane Rep. at 10, 11, 36; Levy Rep. at 14; Singh Rep. at 19, 59).

135 *Id*.

study authors or plaintiffs' experts draw from it. For example, as detailed in the reports of Drs. Birrer, Neel and Kurman:

- The authors of the study used a granulosa cell line, which is irrelevant to epithelial ovarian cancer.[136]
- The "normal" ovarian cells tested were not actually normal, but were instead "immortalized" by some undocumented method that could affect the reaction observed.[137]
- The effects of talc purportedly observed by the authors were "minimal, time-dependent and divergent depending upon dose."[138] Specifically, the increase in cells observed at 24 hours disappeared at 72 hours.[139] In addition, high concentrations of talc were observed to result in inhibition on control cells, while lower concentrations are reported to be stimulatory – an anomalous result.[140] There are no data to explain any of these results.
- The only measure of cellular transformation used by the authors was soft agarose growth and it is well known that this can provide misleading results in that many human tumors do not grow in these conditions, while non-transformed cells can.[141] Further, the results were conflicting between the two cell lines used – in one cell line, a high dose of talc suppressed soft agarose growth, but in the other cell line, it promoted soft agarose growth.[142]
- The paper reports that "[t]alc caused an initial dose-dependent decrease in ROS [Reactive Oxygen Species] generation (24 h) which

---

136 (*See* Birrer Rep. at 14; Neel Rep. at 25; Kurman Rep. at 18.)

137 (Birrer Rep. at 14; Neel Rep. at 25; Kurman Rep. at 18.)

138 (Birrer Rep. at 15; *see also* Neel Rep. at 25.)

139 (Birrer Rep. at 15.)

140 (*Id.*)

141 (Neel Rep. at 25-26; Birrer Rep. at 15.)

142 (*See* Kurman Rep. at 18.)

increased with time in [certain] cells,"[143] but the data do not support that statement. Instead, all doses and time points except one remained below the control levels.[144] Thus, the data indicate that the "general effect of talc was to decrease ROS relative to controls" – not to increase it – "and it was this effect that changed over time."[145]

- The study did not use any control particles (i.e., non-talc particles of approximately the same size), which would help determine whether any effects of exposure were attributable to talc specifically or instead to the physical size and shape of the particles (in which case any effects of exposure would not be specific to talc).[146]

In short, the Buz'Zard study does not provide a reliable basis for plaintiffs' experts' inflammation hypothesis. Indeed, while the article was published more than a decade ago, there is still no general scientific acceptance of the proposition that talc use fosters an inflammatory process that leads to ovarian cancer, underscoring the fact that the scientific community has not interpreted its findings as demonstrating a biological mechanism.[147]

---

143 Buz'Zard & Lau 2007 at 582.

144 (Birrer Rep. at 15.)

145 (*Id*. (emphasis omitted).)

146 (*Id.*; *see also* Kurman Rep. at 18.)

147 (*See* Birrer Rep. at 15.) In support of his inflammation opinions, Dr. Saed also cites Shukla et al., *Alterations in Gene Expression in Human Mesothelial Cells Correlate with Mineral Pathogenicity*, 41(1) Am J Respir Cell Mol Biol. 114 (2009) (attached as Ex. A131 to Tersigni Cert.). But this study does not support plaintiffs' experts' conclusions because it addresses gene expression – which does not by itself say anything about the ostensible carcinogenicity of talc – and focuses largely on mesothelial cells and asbestos. (*See* Birrer Rep. at 16.) To the limited extent the study addressed talc and ovarian cells, it showed no effect on gene expression. (*Id*.) As one of the study authors, defense expert Dr. Mossman,

(cont'd)

Second, plaintiffs' experts attempt to support the inflammation theory by arguing that certain inflammatory conditions – pelvic inflammatory disease ("PID") and endometriosis – are associated with an increased risk of ovarian cancer and that use of anti-inflammatory drugs (NSAIDs and/or aspirin) are associated with a decreased ovarian cancer risk.[148] But plaintiffs' experts mischaracterize the studies they cite and ignore others that refute these putative links.

There have been multiple studies of the incidence of certain subtypes of ovarian cancer in women with PID – an infection of the tubes and ovaries usually from a sexually transmitted disease – and they have had inconsistent results.[149]

(cont'd from previous page)
explained at her deposition, the experiment did not "attempt[] to show changes with talc carcinogenicity"; talc was simply used as a control. (Mossman Dep. 362:14-16.)

148 (*See, e.g.*, Kane Rep. at 35 (supporting inflammation theory by stating that PID and endometriosis "are known risk factors for ovarian cancer"); Singh Rep. at 58 (similar); Zelikoff Rep. at 21-22 (supporting inflammation theory with analogy to "endometriosis and pelvic inflammatory disease[,] which are all associated with induction of local cancer"); Smith-Bindman Rep. at 12 ("[T]here are well described and accepted causal pathways linking inflammation in the etiology of . . . ovarian cancer (pelvic inflammatory disease and endometriosis)".); McTiernan Rep. at 60 ("Further evidence of the inflammation mechanism comes from studies which evaluate anti-inflammatories, like aspirin and NSAIDs . . . ."); Smith Rep. at 17-18 (opining that "[t]he inflammatory basis for cancer development is also supported by studies showing a reduced risk of cancer with the use of anti-inflammatory agents," though later conceding that these data are "somewhat inconsistent"); Wolf Rep. at 12; Levy Rep. at 12-13 (both similar).)

149 (*See* Birrer Rep. at 17.)

While a recent nationwide cohort study in Taiwan demonstrated an association between PID and ovarian cancer, the study had only a three-year follow-up, meaning that many of the cancers may have been present at the same time as PID.[150] As Dr. Birrer has explained, this "is a serious flaw because it begs the question: Did PID increase the risk of ovarian cancer or did the cancer increase the risk of PID?"[151] As noted above, other studies have concluded that the association of PID with ovarian cancer risk is **limited to borderline tumors and, potentially, low-grade serous carcinomas** – and, in any event, requires further investigation.[152]

---

150 Lin et al., *Risk of Ovarian Cancer in Women with Pelvic Inflammatory Disease: A Population-Based Study*, 12(9) Lancet Oncol. 900 (2011) (attached as Ex. A90 to Tersigni Cert.).

151 (Birrer Rep. at 18.)

152 *See* Rasmussen et al., *Pelvic Inflammatory Disease and the Risk of Ovarian Cancer and Borderline Ovarian Tumors: A Pooled Analysis of 13 Case-Control Studies*, 185(1) Am J Epidemiol. 8 (2017) (attached as Ex. A116 to Tersigni Cert.). Plaintiffs' experts' reliance on Balkwill and Mantovani's outdated 2001 paper "Inflammation and Cancer: Back to Virchow?" for the proposition that "[c]hronic inflammation, and even subtle, subclinical inflammation, is associated with an increased risk of cancer" (Smith-Bindman Rep. at 12; *see also* Zelikoff Rep. at 21) is similarly misplaced. The article, which was written more than 15 years ago, does not reflect current scientific knowledge regarding the origins of ovarian cancer; it merely presents a hypothesis regarding inflammation and cancers generally. As Dr. Neel explained, "[t]here[ha]s been more learned about ovarian cancer in the last ten years than in all of reported history before then." (*See* Dep. of Benjamin Neel, M.D., Ph.D. 127:15-18, Mar. 19, 2019 (attached as Ex. B6 to Tersigni Cert.).) In any event, to the extent the Balkwill and Mantovani paper addresses ovarian cancer, it is to summarily state in a chart – without any citation – *(cont'd)*

Similarly, as explained above, endometriosis – another inflammatory condition that plaintiffs' experts cite as being associated with ovarian cancer[153] – "**is not** associated with an increased risk of" HGSOC.[154] Instead, endometriosis is associated only with the endometrioid carcinoma ("EC") and clear cell carcinoma ("CCC") varieties of ovarian cancer,[155] and the mechanism by which it is thought to lead to cancer ***is not inflammation***, as discussed above. (*See* p. 14, supra.) In addition, EC and CCC tumors "arise from different locations and cell types" than HGSOC.[156] Thus, any association between endometriosis and EC and CCC, specifically, could not be indicative of a link between inflammation and ovarian cancer generally. Plaintiffs' own experts have testified similarly. For example, Dr. Kane could not identify any ovarian cancer subtypes that have been causally associated with chronic inflammation in the published literature other than CCC and has admitted that she did not "believe that the mechanisms of all of these

---

(cont'd from previous page)
that "ovarian" cancer has been associated with "inflammatory stimulus," including PID and talc. But, as set forth above, PID has only been potentially connected to borderline tumors and, potentially, low-grade serous carcinoma, not HGSOC. Further, the article contains no scientific basis for connecting talc to chronic inflammation capable of causing any type of ovarian cancer.

153 (Smith Rep. at 3; Clarke-Pearson Rep. at 5; Kane Rep. at 10, 12-13, 35; Levy Rep. at 12; McTiernan Rep. at 60; Singh Rep. at 58; Smith-Bindman Rep. at 11-12; Wolf Rep. at 4; Zelikoff Rep. at 21.)

154 (Birrer Rep. at 18 (emphasis added); *see also* Neel Rep. at 13.)

155 (Birrer Rep. at 18.)

156 (*Id.*)

tumors have been elucidated completely."[157] In addition, Dr. Kane conceded that different ovarian cancer subtypes behave differently, and it is unclear whether they have the same origins.[158]

The alleged association between the use of NSAIDs or aspirin and a decreased risk of ovarian cancer on which several plaintiffs' experts rely[159] also does not support their hypothesis that any subtype of ovarian cancer results from inflammation. In fact, a large meta-analysis of multiple epidemiologic studies examining the association of NSAIDs/aspirin use with ovarian cancer risk (including every relevant study conducted through 2012) found that there is ***no statistically significant association*** between NSAID use and the prevention of ovarian cancer.[160] "Based on this meta-analysis," the authors expressly concluded that "the association between aspirin and non-aspirin NSAID use and ovarian

---

157 (Dep. of Sarah E. Kane, M.D. 67:2-4, Jan. 25, 2019 (attached as Ex. B45 to Tersigni Cert.).)

158 (*Id.* 88:3-23; 88:24-89:24.)

159 (Smith Rep. at 18; Kane Rep. at 12; McTiernan Rep. at 60; Levy Rep. at 12-13; Wolf Rep. at 12.)

160 *See* Baandrup et al., *Nonsteroidal Anti-Inflammatory Drugs and Risk of Ovarian Cancer: Systematic Review and Meta-Analysis of Observational Studies*, 92(3) Acta Obstet Gynecol Scand. 245 (2013) ("Baandrup 2013") (attached as Ex. A9 to Tersigni Cert.); *see also* Bonovas et al., *Do Nonsteroidal Anti-Inflammatory Drugs Affect the Risk of Developing Ovarian Cancer? A Meta-Analysis*, 60(2) Br J Clin Pharmacol. 194 (2005) (attached as Ex. A12 to Tersigni Cert.); Ni et al., *Meta-Analysis on the Association Between Non-Steroidal Anti-Inflammatory Drug Use and Ovarian Cancer*, 75(1) Br J Clin Pharmacol. 26 (2012) (attached as Ex. A107 to Tersigni Cert.).

cancer risk is weak."[161] Plaintiffs' experts generally ignore these findings,[162] offering yet another example of their willful blindness to "contrary evidence." *Zoloft*, 26 F. Supp. 3d at 461.

In fact, as Dr. Smith acknowledges, the studies on which plaintiffs' experts rely show "inconsistent" results as to the effect of anti-inflammatory drugs on ovarian cancer risk.[163] For example, one of the studies plaintiffs' experts cite – a recent meta-analysis by Trabert and others of 16 cohort studies – reported a modest (10%, barely statistically significant) risk reduction with daily aspirin use for less than 10 years.[164] But the same study also found that other types of anti-inflammatory drug use (including use of NSAIDs and acetaminophen, and long-term aspirin use) either did not affect ovarian cancer risk or were associated with a non-statistically significant ***increase*** in risk.[165] These results are difficult to square

---

161 Baandrup 2013 at 245 (abstract).

162 Only Dr. Kane cites the Baandrup study, ostensibly as "further support[] [for] the role of inflammation in carcinogenesis," and she fails to mention its findings refuting a protective role for NSAIDs. (*See* Kane Rep. at 12.)

163 (Smith Rep. at 18 ("Although somewhat inconsistent, data regarding NSAID and aspirin use suggest a protective effect (results of these studies are inconsistent[])."); *see also* Wolf Rep. at 12 ("somewhat contradictory" results).)

164 Trabert et al., *Analgesic Use and Ovarian Cancer Risk: An Analysis in the Ovarian Cancer Cohort Consortium*, 111(2) J. Nat'l Cancer Inst. 137, 139-42 (2019) (attached as Ex. A141 to Tersigni Cert.) (cited in Smith Rep. at 18; Wolf Rep. at 12).

165 *Id.* at 142. Plaintiffs' experts additionally cite an earlier Trabert meta-analysis (of 12 case-control studies), which reported a larger reduction of risk with *(cont'd)*

with plaintiffs' experts' argument that anti-inflammatory drugs decrease ovarian cancer risk and not surprisingly, anti-inflammatory drugs are not recommended in clinical practice to reduce patients' risk of ovarian cancer.[166]

In short, plaintiffs' experts are unable to point to any reliable scientific evidence that there is a biologically plausible connection between chronic inflammation and ovarian cancer – and the established science weighs against their hypothesis.[167] For this reason, too, plaintiffs' experts' biological plausibility opinions should be excluded under *Daubert*.

B. Plaintiffs' Experts' Theory That Perineal Talc Use Increases The Risk of Ovarian Cancer By Inhibiting MUC1 Antibodies Is Not Biologically Plausible.

Two of plaintiffs' experts – Drs. Zelikoff and Saed – have alternatively suggested that talc use causes ovarian cancer by lowering the body's MUC1

(cont'd from previous page)
aspirin use but similarly inconsistent results for other types of anti-inflammatory drugs. *See* Trabert et al., *Aspirin, Nonaspirin Nonsteroidal Anti-Inflammatory Drug, and Acetaminophen Use and Risk of Invasive Epithelial Ovarian Cancer: A Pooled Analysis in the Ovarian Cancer Association Consortium*, 106(2) J. Nat'l Cancer Inst. 1 (2014) (attached as Ex. A142 to Tersigni Cert.) (cited in Levy Rep. at 13; Kane Rep. at 12; Smith Rep. at 18; McTiernan Rep. at 60).

166 (Holcomb Rep. at 18; Expert Report of Cheryl Christine Saenz, M.D. at 20, Feb. 25, 2019 (attached as Ex. C12 to Tersigni Cert.).)

167 Notably, plaintiffs' experts also do not cite any animal studies that have shown that talc exposure caused ovarian cancer; nor could they. As Dr. Neel put it, "***no animal studies have shown that ovarian cancer develops following talc injection***." (Neel Rep. at 21.)

antibodies.[168] Specifically, these experts claim that talcum powder users have lower plasma levels of MUC1 antibodies than non-users and propose that decreased immunity to MUC1 could be a mechanism by which talc increases ovarian cancer risk.[169] This is pure speculation.

MUC1 is a membrane-bound glycoprotein present on most epithelial cells, the overexpression of which is a "prominent characteristic of various types of cancers and inflammatory diseases," including ovarian cancer.[170] According to Dr. Zelikoff, "[r]educing immunity to MUC-1 could be one mechanism by which talc increases endometrial and/or ovarian cancer risk."[171]

But the only study Dr. Zelikoff cites to support her MUC1 theory investigated the potential association between talc and endometrial, ***not ovarian***, cancer – and found no statistical association.[172] Moreover, even if there were reliable evidence of an association between talc use and a patient's level of

---

168 (*See* Zelikoff Rep. at 19; Saed Rep. at 12.)

169 (*Id*.)

170 (*See* Expert Report of H. Nadia Moore, Ph.D., D.A.B.T., E.R.T. ("Moore Rep.") at 37, Feb. 25, 2019 (attached as Ex. C19 to Tersigni Cert.) (quoting Bafna et al., *Membrane-Bound Mucins: The Mechanistic Basis for Alterations in the Growth and Survival of Cancer Cells*, 29(20) Oncogene 2893 (2010) and citing other sources).)

171 (*See* Zelikoff Rep. at 19 (citing Karageorgi et al., *Perineal Use of Talcum Powder and Endometrial Cancer Risk*, 19(5) Cancer Epidemiol Biomarkers Prev. 1269 (2010) ("Karageorgi 2010")) (attached as Ex. A84 to Tersigni Cert.).)

172 *See* Karageorgi 2010.

circulating anti-MUC1 antibodies, it would be irrelevant because there is no evidence that circulating anti-MUC1 antibodies actually affect ovarian cancer risk. Not one of plaintiffs' experts in this litigation proposes any relationship between MUC1 antibodies and the development of cancer.

By contrast, defense experts have made clear that MUC1 is ***not*** involved in anti-tumor immunity, which is mediated by other types of cells. As Dr. Neel explains, "[a]nti-tumor immunity is primarily mediated by anti-tumor T lymphocytes and possibly NK cells," and there is "no evidence that anti-MUC1 antibodies (which are produced by B-lymphocytes) play any role in immune surveillance of ovarian or other types of cancer."[173] Accordingly, plaintiffs' experts' MUC1 theory of "ovarian cancer risk is scientifically flawed and methodologically invalid."[174] *See Henricksen*, 605 F. Supp. 2d at 1175 (excluding causation opinions where plaintiffs' experts could not overcome "the overwhelming body of contradictory and inconsistent" evidence on the issue; "[i]n deciding whether the Plaintiffs' expert opinions have adequate scientific

---

[173] (Neel Rep. at 23; *see also* Moore Rep. at 37 ("[A]ny potential association between circulating anti-MUC1 antibodies and subsequently developing ovarian cancer is unknown").)

[174] (Moore Rep. at 37; *see also* Neel Rep. at 23 (noting that plaintiffs' MUC1 theory "should be viewed as pure speculation").)

foundation, the court" considers "evidence proffered by the defense and defense experts").

IV. DR. ZELIKOFF'S BIOLOGICAL PLAUSIBILITY AND OTHER OPINIONS SHOULD BE SEPARATELY EXCLUDED BECAUSE OF HER RAMPANT PLAGIARISM.

Dr. Zelikoff's opinions are also unreliable because significant portions of her expert report are plagiarized from other sources. *See, e.g.*, *Moore v. BASF Corp.*, No. 11-1001, 2012 WL 6002831, at *7 (E.D. La. Nov. 30, 2012) (finding that "[t]he likelihood that substantial portions of Dr. Kura's report do not reflect his original work is yet another reason that the [c]ourt finds that Dr. Kura's opinions in general are unreliable"), *aff'd sub nom. Moore v. Int'l Paint, L.L.C.*, 547 F App'x 513 (5th Cir. 2013) (per curiam).

At her deposition, Dr. Zelikoff conceded that numerous portions of her report are copied verbatim from other sources without quotation marks or credit to the source.[175] In addition, Dr. Zelikoff's report contains several identical sentences

[175] (*See, e.g.*, Zelikoff Dep. 96:8-97:2 (admitting that portions of Genetic Home Reference were copied verbatim in her report without quotation marks or acknowledgment); *id.* 102:21-106:8 (acknowledging that several sentences from Simone Reuter article were copied without quotation or acknowledgment); *id.* 107:14-109:22 (acknowledging that five portions of EnvironmentalChemistry.com are copied verbatim in her report); *id.* 115:17-119:17 (defending copying of four sentences of Rakoff-Nahoum publication by claiming, incorrectly, that author she copied also did not give references); *id.* 119:22-121:13 (acknowledging having copied language from OSHA publication without citation).)

and paragraphs to those contained in Dr. Levy's and Dr. Cook's reports (which Drs. Levy and Cook testified that Dr. Zelikoff must have taken from their reports).

Critically, the plagiarized portions of Dr. Zelikoff's report do not go to mere background points; nor are they stray sentences where attribution or quotation marks were plausibly omitted by mistake. Rather, the copied passages – some of which are a paragraph in length – relate to core issues such as the carcinogenicity of nickel and the origins of genetic mutations and their relationship to disease risk.[176] Moreover, some of the passages – like the ones on genetics – are taken from websites, rather than published, peer-reviewed literature.[177]

Dr. Zelikoff's plagiarism not only constitutes research misconduct, but also greatly compromises the integrity of her opinions.[178] As such, her opinions are unreliable for this reason was well and must be excluded.[179]

---

176 (*See* Moore Rep. at 100-03 (illustrating these examples).)

177 (*See id.* at 102-03 (noting material taken from a website providing genetics explanations for a lay audience).)

178 *See generally* Executive Office of the President; Federal Policy on Research Misconduct; Preamble for Research Misconduct Policy, 65 Fed. Reg. 76,260, 76,262 (Dec. 6, 2000) (defining "[r]esearch misconduct" as "plagiarism in proposing, performing, or reviewing research, or in reporting research results" and defining plagiarism as "the appropriation of another person's ideas, processes, results, or words without giving appropriate credit").

179 A number of plaintiffs' other experts similarly copied sections of their reports from sources they failed to attribute. For example, although Dr. Levy testified that the words in his report were his own (Dep. of Shawn Levy, Ph.D. 48:13-22, Jan. 11, 2019 (attached as Ex. B46 to Tersigni Cert.)), he was forced to

(cont'd)

CONCLUSION

For the reasons set forth above, the Court should exclude plaintiffs' experts' biological plausibility opinions.

Dated: May 7, 2019

Respectfully submitted,

/s/ Susan M. Sharko
Susan M. Sharko
DRINKER BIDDLE & REATH LLP
600 Campus Drive
Florham Park, New Jersey 07932
Telephone: 973-549-7000
Facsimile: 973-360-9831
E-mail: susan.sharko@dbr.com

John H. Beisner
Jessica D. Miller
SKADDEN, ARPS, SLATE,
MEAGHER & FLOM LLP

(cont'd from previous page)

concede at his deposition that portions of his report are "identical" to a Wikipedia webpage about the BRCA1 gene (*id.* 72:6-73:19). He further "agree[d]" that four sentences in his report are identical to ones found on the Mayo Clinic's website about cancer (*id.* 60:20-66:10); and that portions of his report are "similar" to sentences in an article by Drs. Lisa Coussens and Zena Werb (*id.* 76:5-79:3). Likewise, although Dr. Crowley agreed that avoiding plagiarism was important in "maintain[ing] scientific integrity" (Dep. of Michael Crowley, Ph.D. 88:3-12, Jan. 4, 2019 (attached as Ex. B37 to Tersigni Cert.)), he conceded that paragraphs of his report were "lifted verbatim" from an article about fragranced consumer products (*id.* 95:10-99:15); a Wikipedia webpage about the mucous membrane (*id.* 100:19-102:9); and a website called Interactive Learning Paradigms Incorporated (*id.* 102:10-104:19). In addition, Drs. McTiernan and Singh both acknowledged that, in view of the word-for-word overlap between portions of their reports and other sources, they "should have cited" the works they copied. (Dep. of Anne McTiernan, M.D., Ph.D. 133:3-137:20, Jan. 28, 2019 (attached as Ex. B2 to Tersigni Cert.); Singh Dep. 245:7-248:8.)

1440 New York Avenue, N.W.
Washington, D.C. 20005
202-371-7000

Attorneys for Defendants Johnson & Johnson and Johnson & Johnson Consumer Inc.